



**PCT**  
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INTERNATIONALE ANMELDUNG VERÖFFENTLICHT NACH DEM VERTRAG ÜBER DIE  
INTERNATIONALE ZUSAMMENARBEIT AUF DEM GEBIET DES PATENTWESENS (PCT)

<b>(51) Internationale Patentklassifikation <sup>6</sup> :</b> <b>C07D 493/04, 417/06, 413/06, 277/24</b>	<b>A2</b>	<b>(11) Internationale Veröffentlichungsnummer: WO 99/65913</b>  <b>(43) Internationales Veröffentlichungsdatum:</b> 23. Dezember 1999 (23.12.99)		
<table style="width: 100%; border: none;"><tr><td style="width: 50%; vertical-align: top; padding: 5px;"><b>(21) Internationales Aktenzeichen:</b> PCT/EP99/04244  <b>(22) Internationales Anmeldedatum:</b> 18. Juni 1999 (18.06.99)  <b>(30) Prioritätsdaten:</b> 198 26 988.9      18. Juni 1998 (18.06.98)      DE  <b>(71) Anmelder (für alle Bestimmungsstaaten ausser US):</b> GESELLSCHAFT FÜR BIOTECHNOLOGISCHE FORSCHUNG MBH (GBF) [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE).  <b>(72) Erfinder; und</b> <b>(75) Erfinder/Anmelder (nur für US):</b> HOEFLE, Gerhard [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE). REICHENBACH, Hans [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE). GERTH, Klaus [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE). HARDT, Ingo [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE). SASSE, Florenz [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE). STEINMETZ, Heinrich [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE).  <b>(74) Anwälte:</b> BOETERS, Hans usw.; Boeters &amp; Bauer, Bereit- eranger 15, D-81541 München (DE).</td><td style="width: 50%; vertical-align: top; padding: 5px;"><b>(81) Bestimmungsstaaten:</b> AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO Patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), eurasisches Patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), europäisches Patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI Patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  <b>Veröffentlicht</b> <i>Ohne internationalen Recherchenbericht und erneut zu veröffentlichen nach Erhalt des Berichts.</i></td></tr></table>			<b>(21) Internationales Aktenzeichen:</b> PCT/EP99/04244  <b>(22) Internationales Anmeldedatum:</b> 18. Juni 1999 (18.06.99)  <b>(30) Prioritätsdaten:</b> 198 26 988.9      18. Juni 1998 (18.06.98)      DE  <b>(71) Anmelder (für alle Bestimmungsstaaten ausser US):</b> GESELLSCHAFT FÜR BIOTECHNOLOGISCHE FORSCHUNG MBH (GBF) [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE).  <b>(72) Erfinder; und</b> <b>(75) Erfinder/Anmelder (nur für US):</b> HOEFLE, Gerhard [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE). REICHENBACH, Hans [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE). GERTH, Klaus [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE). HARDT, Ingo [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE). SASSE, Florenz [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE). STEINMETZ, Heinrich [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE).  <b>(74) Anwälte:</b> BOETERS, Hans usw.; Boeters & Bauer, Bereit- eranger 15, D-81541 München (DE).	<b>(81) Bestimmungsstaaten:</b> AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO Patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), eurasisches Patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), europäisches Patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI Patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  <b>Veröffentlicht</b> <i>Ohne internationalen Recherchenbericht und erneut zu veröffentlichen nach Erhalt des Berichts.</i>
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<b>(54) Title:</b> EPOTHILONE MINOR CONSTITUENTS  <b>(54) Bezeichnung:</b> EPOTHILON-NEBENKOMPONENTEN  <b>(57) Abstract</b>  The invention relates to compounds which are obtained by fermenting DSM 6773, especially epothilones A1, A2, A8, A9, B10, C1, C2, C3, C4, C5, C6, C7, C8, C9, D1, D2, D5, G1, G2, H1, H2, I1, I2, I3, I4, I5, I6 and K and trans-epothilones C1 and C2.  <b>(57) Zusammenfassung</b>  Die Erfindung betrifft Verbindungen, die durch Fermentation von DSM 6773 erhältlich sind, insbesondere Epothilone A1, A2, A8, A9, B10, C1, C2, C3, C4, C5, C6, C7, C8, C9, D1, D2, D5, G1, G2, H1, H2, I1, I2, I3, I4, I5, I6 und K und Trans-Epothilone C1 und C2.				

### LEDIGLICH ZUR INFORMATION

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EE	Estland						

### Epothilon-Nebenkomponenten

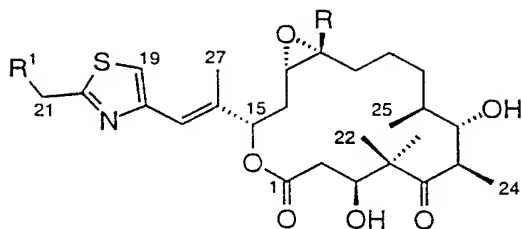
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Die Erfindung betrifft Verbindungen, die im vorliegenden Zusammenhang als Epothilon-Nebenkomponenten bezeichnet werden, und zwar Verbindungen 5 bis 13 und 16 bis 39. Diese Verbindungen lassen sich durch Fermentation von DSM 6773 gemäß DE 41 38 042.8 gewinnen.

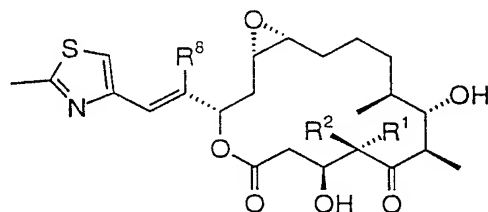
Kenndaten der erfindungsgemäßen Verbindungen sind im folgenden zusammengestellt.

Gewinnung: Die Aufarbeitung eines Rohepothilon-Gemischs, das durch Fermentation von DSM 6773 in einem 900 Liter-Fermentator gewonnen wurde, ist schematisch Fig. 1 bis 2 zu entnehmen.

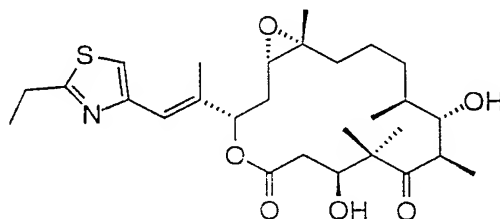
Aktivitäten: vgl. Tab. 1



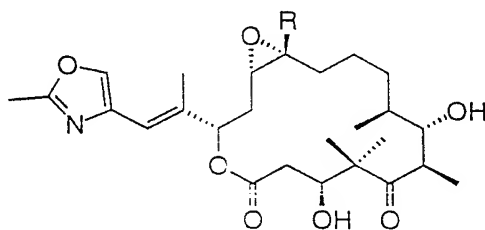
- Epothilone A (1)  $R^1 = H$ ;  $R = H$   
 Epothilone B (2)  $R^1 = H$ ;  $R = Me$   
 Epothilone E (3)  $R^1 = OH$ ;  $R = H$   
 Epothilone F (4)  $R^1 = OH$ ;  $R = Me$



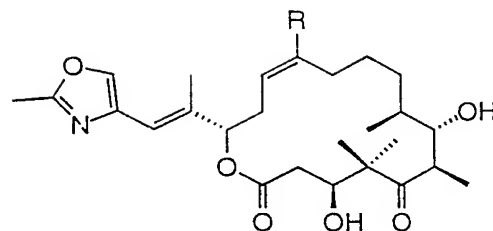
- Epothilone A₁ (5)  $R^1 = H$ ;  $R^2, R^8 = Me$   
 Epothilone A₂ (6)  $R^2 = H$ ;  $R^1, R^8 = Me$   
 Epothilone A₈ (7)  $R^8 = H$ ;  $R^1, R^2 = Me$   
 Epothilone A₉ (8)  $R^1 = CH_2OH$ ;  $R^2, R^8 = Me$



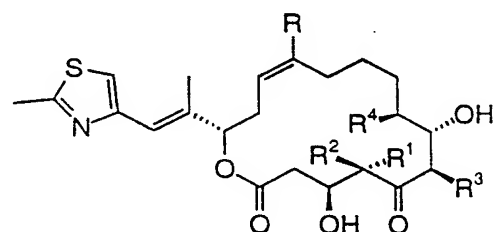
Epothilone B₁₀ (9)



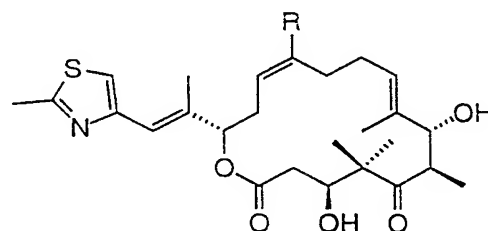
- Epothilone G₁ (10)  $R = H$   
 Epothilone G₂ (11)  $R = Me$



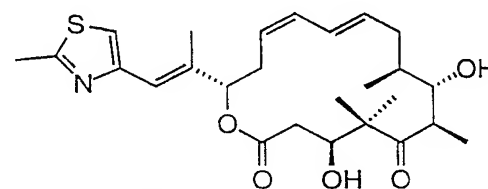
- Epothilone H₁ (12)  $R = H$   
 Epothilone H₂ (13)  $R = Me$



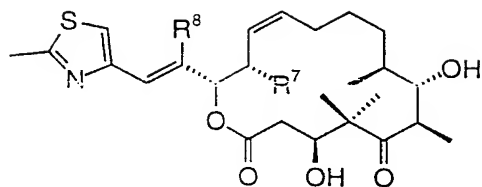
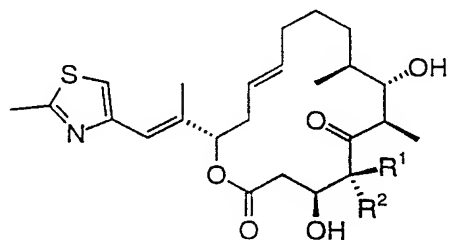
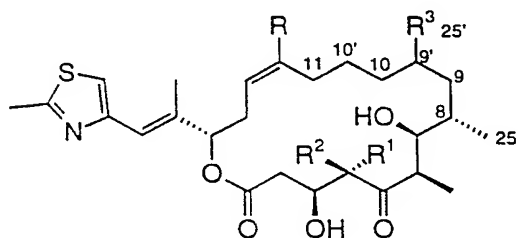
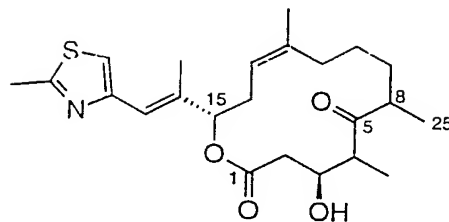
- Epothilone C (14)  $R^1, R^2, R^3, R^4 = Me$ ;  $R = H$   
 Epothilone D (15)  $R^1, R^2, R^3, R^4, R = Me$   
 Epothilone C₁ (16)  $R^1 = H$ ;  $R^2, R^3, R^4 = Me$ ;  $R = H$   
 Epothilone D₁ (17)  $R^1 = H$ ;  $R^2, R^3, R^4 = Me$ ;  $R = Me$   
 Epothilone C₂ (18)  $R^2 = H$ ;  $R^1, R^3, R^4 = Me$ ;  $R = H$   
 Epothilone D₂ (19)  $R^2 = H$ ;  $R^1, R^3, R^4 = Me$ ;  $R = Me$   
 Epothilone C₃ (20)  $R^3 = H$ ;  $R^1, R^2, R^4 = Me$ ;  $R = H$   
 Epothilone C₄ (21)  $R^4 = H$ ;  $R^1, R^2, R^3 = Me$ ;  $R = H$



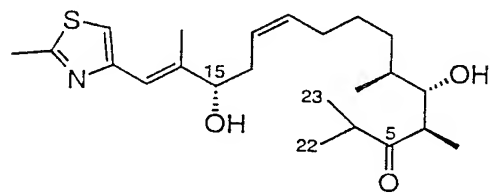
- Epothilone C₅ (22)  $R = H$   
 Epothilone D₅ (23)  $R = Me$



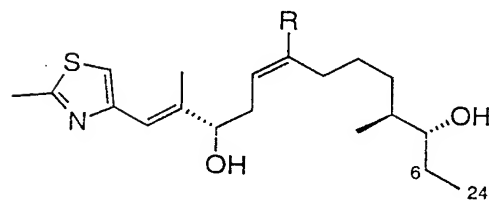
Epothilone C₆ (24)

Epothilone C<sub>7</sub> (25) R<sup>7</sup> = OH; R<sup>8</sup> = MeEpothilone C<sub>8</sub> (26) R<sup>8</sup>, R<sup>7</sup> = HEpothilone C<sub>9</sub> (27) R<sup>8</sup> = CH<sub>2</sub>OH; R<sup>7</sup> = Htrans-Epothilone C<sub>1</sub> (28) R<sup>1</sup> = H; R<sup>2</sup> = Metrans-Epothilone C<sub>2</sub> (29) R<sup>2</sup> = H; R<sup>1</sup> = MeEpothilone I<sub>1</sub> (30) R, R<sup>3</sup> = H; R<sup>1</sup>, R<sup>2</sup> = MeEpothilone I<sub>2</sub> (31) R = H; R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup> = MeEpothilone I<sub>3</sub> (32) R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R = MeEpothilone I<sub>4</sub> (33) R<sup>2</sup>, R = H; R<sup>1</sup>, R<sup>3</sup> = MeEpothilone I<sub>5</sub> (34) R<sup>2</sup> = H; R<sup>1</sup>, R<sup>3</sup>, R = MeEpothilone I<sub>6</sub> (35) R<sup>1</sup> = H; R<sup>2</sup>, R<sup>3</sup>, R = Me

Epothilone K (36)



(37)



(38) R = H

(39) R = Me

**Epothilone A<sub>1</sub> (5):** colorless amorphous solid;  $[\alpha]_D^{22}$  -69 (*c* 0.1, MeOH); UV (MeOH)  $\lambda_{\max}$  nm ( $\epsilon$ ) 208 (19600), 247 (13600); IR (KBr)  $\nu_{\max}$  3437, 2959, 2931, 2876, 1732, 1710, 1455, 1259, 978  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  6.95 (1H, s, H-19), 6.60 (1H, bs, H-17), 5.68 (1H, dd,  $J$  = 4.4, 4.0 Hz, H-15), 4.12 (1H, m, H-3), 3.71 (1H, m, H-7), 3.52 (1H, bs, 7-OH), 3.37 (1H, bd,  $J$  = 7.5 Hz, 3-OH), 3.21 (1H, dq,  $J$  = 7.7, 7.0 Hz, H-4), 3.02 (1H, ddd,  $J$  = 9.2, 4.5, 2.8 Hz, H-13), 2.87 (1H, ddd,  $J$  = 8.3, 4.5, 3.7 Hz, H-12), 2.78 (1H, dd,  $J$  = 16.8, 4.3 Hz, H-2a), 2.70 (3H, s, H-21), 2.66 (1H, dq,  $J$  = 3.9, 7.0 Hz, H-6), 2.65 (1H, dd,  $J$  = 16.8, 5.2 Hz, H-2b), 2.16 (1H, ddd,  $J$  = 15.4, 4.4, 2.8 Hz, H-14a), 2.12 (3H, bs, H-27), 1.91 (1H, ddd,  $J$  = 15.4, 9.2, 4.0 Hz, H-14b), 1.63 (1H, m, H-10a), 1.62 (2H, m, H-11), 1.59 (1H, m, H-9a), 1.52 (1H, m, H-10b), 1.39 (1H, m, H-8), 1.35 (1H, m, H-9b), 1.211 (3H, d,  $J$  = 7.0 Hz, H-23), 1.207 (3H, d,  $J$  = 7.0 Hz, H-24), 0.89 (3H, d,  $J$  = 6.9 Hz, H-25); EIMS  $m/z$  479  $[\text{M}]^+$  (21), 322 (31), 306 (65), 304 (47), 168 (45), 166 (73), 164 (100), 151 (30), 140 (35); HREIMS  $m/z$  479.2317 (calcd. for  $\text{C}_{27}\text{H}_{41}\text{NO}_5\text{S}$ , 479.2342).

**Epothilone A<sub>2</sub> (6):** colorless amorphous solid;  $[\alpha]_D^{22}$  +12.0 (*c* 1.0, MeOH); UV (MeOH)  $\lambda_{\max}$  nm ( $\epsilon$ ) 210 (15100), 248 (15500); IR (KBr)  $\nu_{\max}$  3438, 2963, 2929, 2875, 1734, 1706, 1458, 1262, 981  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  6.98 (1H, s, H-19), 6.63 (1H, bs, H-17), 5.40 (1H, dd,  $J$  = 8.3, 3.4 Hz, H-15), 4.26 (1H, ddd,  $J$  = 8.5, 4.8, 4.7 Hz, H-3), 3.85 (1H, dd,  $J$  = 7.9,

2.6 Hz, H-7), 3.54 (1H, bs, 3-OH), 3.09 (1H, dq,  $J = 4.8, 7.0$  Hz, H-4), 3.01 (1H, ddd,  $J = 8.3, 4.8, 4.6$  Hz, H-13), 2.98 (1H, dq,  $J = 7.9, 7.0$  Hz, H-6), 2.89 (1H, ddd,  $J = 6.7, 4.6, 4.4$  Hz, H-12), 2.68 (3H, s, H-21), 2.60 (1H, dd,  $J = 15.1, 8.5$  Hz, H-2a), 2.52 (1H, bs, 7-OH), 2.50 (1H, dd,  $J = 15.1, 4.7$  Hz, H-2b), 2.18 (1H, ddd,  $J = 15.0, 4.8, 3.4$  Hz, H-14a), 2.11 (3H, d,  $J = 1.3$  Hz, H-27), 1.82 (1H, ddd,  $J = 15.0, 8.3, 8.1$  Hz, H-14b), 1.63 (1H, m, H-8), 1.61 (2H, m, H-11a and H-10a), 1.46 (1H, m, H-11b), 1.39 (2H, m, H-9), 1.31 (1H, m, H-10b), 1.22 (3H, d,  $J = 7.0$  Hz, H-24), 1.15 (3H, d,  $J = 7.0$  Hz, H-22), 1.01 (3H, d,  $J = 6.9$  Hz, H-25);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  216.2 (s, C-5), 170.1 (s, C-1), 164.9 (s, C-20), 152.0 (s, C-18), 137.0 (s, C-16), 120.3 (d, C-17), 116.5 (d, C-19), 76.7 (d, C-15), 75.6 (d, C-7), 69.1 (d, C-3), 57.1 (d, C-12), 54.3 (d, C-13), 50.3 (d, C-4), 49.6 (d, C-6), 39.4 (t, C-2), 35.5 (d, C-8), 32.2 (t, C-14), 29.6 (t, C-9), 27.6 (t, C-11), 23.9 (t, C-10), 19.2 (q, C-21), 18.0 (q, C-25), 15.6 (q, C-27), 13.9 (q, C-24), 12.4 (q, C-22); EIMS  $m/z$  479  $[\text{M}]^+$  (18), 322 (38), 306 (78), 304 (59), 168 (48), 166 (96), 164 (100), 151 (33), 140 (38); HREIMS  $m/z$  479.2318 (calcd. for  $\text{C}_{27}\text{H}_{41}\text{NO}_5\text{S}$ , 479.2342).

**Epithilone A<sub>5</sub> (7):** colorless amorphous solid;  $[\alpha]_D^{22} -76.2$  ( $c$  1.0, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) 210 (15300), 248 (15500); IR (KBr)  $\nu_{\text{max}}$  3440, 2967, 2932, 2876, 1736, 1691, 1467, 1252, 979  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  6.95 (1H, s, H-19), 6.64 (1H, dd,  $J = 15.6, 0.9$  Hz, H-17), 6.52 (1H, dd,  $J = 15.6, 6.6$  Hz, H-16), 5.68 (1H, dddd,  $J = 7.8, 6.6, 3.2, 0.9$  Hz, H-15), 4.11 (1H, ddd,  $J = 10.1, 6.6, 3.5$  Hz, H-3), 3.78 (1H, ddd,  $J = 5.2, 3.2, 3.2$  Hz, H-7), 3.66 (1H, d,  $J = 6.6$  Hz, 3-OH), 3.23 (1H, dq,  $J = 5.2, 6.9$  Hz, H-6), 3.08 (1H, ddd,  $J = 7.3, 5.5, 4.1$  Hz, H-13), 2.90 (1H, ddd,  $J = 6.6, 4.6, 4.1$  Hz, H-12), 2.69 (3H, s, H-21), 2.52 (1H, dd,  $J = 14.7, 10.1$  Hz, H-2a), 2.44 (1H, bd,  $J = 3.2$  Hz, 7-OH), 2.41 (1H, dd,  $J = 14.7, 3.5$  Hz, H-2b), 2.10

(1H, ddd,  $J = 15.0, 5.5, 3.2$  Hz, H-14a), 1.90 (1H, ddd,  $J = 15.0, 7.8, 7.3$  Hz, H-14b), 1.71 (1H, m, H-8), 1.65 (1H, m, H-11a), 1.50 (1H, m, H-10a), 1.47 (1H, m, H-11b), 1.40 (2H, m, H-9), 1.39 (1H, m, H-10b), 1.33 (3H, s, H-23), 1.16 (3H, d,  $J = 6.9$  Hz, H-24), 1.08 (3H, s, H-22), 0.98 (3H, d,  $J = 7.0$  Hz, H-25);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  220.3 (s, C-5), 170.7 (s, C-1), 166.5 (s, C-20), 152.2 (s, C-18), 128.4 (d, C-16), 125.9 (d, C-17), 116.4 (d, C-19), 75.0 (d, C-7), 73.6 (d, C-3), 72.7 (d, C-15), 57.3 (d, C-12), 54.1 (d, C-13), 52.6 (s, C-4), 43.8 (d, C-6), 38.9 (t, C-2), 36.3 (d, C-8), 32.5 (t, C-14), 30.3 (t, C-9), 26.7 (t, C-11), 24.0 (t, C-10), 21.3 (q, C-23), 21.0 (q, C-22), 19.3 (q, C-21), 17.1 (q, C-25), 14.5 (q, C-24); EIMS  $m/z$  479  $[\text{M}]^+$  XXX; HRDCIMS  $m/z$  480.2401 (calcd. for  $\text{C}_{25}\text{H}_{38}\text{NO}_6\text{S}$ , 480.2401).

**Epothilone A<sub>9</sub> (8):** colorless amorphous solid;  $[\alpha]_{\text{D}}^{22} -37.6$  ( $c$  0.5, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) 211 (15500), 253 (14100); IR (KBr)  $\nu_{\text{max}}$  3423, 2965, 2932, 2877, 1736, 1690, 1463, 1249, 1014, 979  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.10 (1H, s, H-19), 6.72 (1H, dd,  $J = 10.7, 4.3$  Hz, 27-OH), 6.60 (1H, bs, H-17), 5.69 (1H, dd,  $J = 11.6, 2.0$  Hz, H-15), 5.59 (1H, d,  $J = 6.6$  Hz, 3-OH), 4.49 (1H, ddd,  $J = 12.9, 4.3, 1.2$  Hz, H-27a), 4.27 (1H, ddd,  $J = 11.6, 6.6, 2.9$  Hz, H-3), 4.11 (1H, ddd,  $J = 12.9, 10.7, 1.0$  Hz, H-27b), 3.71 (1H, ddd,  $J = 4.8, 3.0, 2.8$  Hz, H-7), 3.17 (1H, dq,  $J = 3.0, 6.8$  Hz, H-6), 3.04 (1H, ddd,  $J = 9.7, 3.6, 2.2$  Hz, H-13), 2.93 (1H, bs, 7-OH), 2.91 (1H, ddd,  $J = 9.7, 3.6, 2.7$  Hz, H-12), 2.72 (3H, s, H-21), 2.48 (1H, dd,  $J = 14.2, 11.6$  Hz, H-2a), 2.11 (1H, dd,  $J = 14.2, 2.9$  Hz, H-2b), 2.03 (1H, ddd,  $J = 14.7, 2.2, 2.0$  Hz, H-14a), 1.86 (1H, m, H-11a), 1.85 (1H, m, H-14b), 1.79 (1H, m, H-8), 1.52 (1H, m, H-10a), 1.37 (3H, m, H-9 and H-10b), 1.37 (3H, s, H-23), 1.36 (1H, m, H-11b), 1.19 (3H, d,  $J = 6.8$  Hz, H-24), 1.02 (3H, d,  $J = 7.1$  Hz, H-25), 1.00 (3H, s, H-22);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  220.5 (s, C-5),



170.2 (s, C-1), 167.5 (s, C-20), 150.7 (s, C-18), 138.9 (s, C-16), 125.2 (d, C-17), 119.5 (d, C-19), 76.7 (d, C-15), 73.4 (d, C-7), 70.4 (d, C-3), 57.7 (d, C-12), 57.2 (t, C-27), 55.3 (d, C-13), 54.2 (s, C-4), 41.3 (d, C-6), 40.7 (t, C-2), 37.5 (d, C-8), 31.8 (t, C-14), 31.2 (t, C-9), 28.0 (t, C-11), 23.7 (q, C-23), 23.2 (t, C-10), 19.2 (q, C-21), 16.8 (q, C-22), 15.8 (q, C-25), 13.5 (q, C-24); EIMS  $m/z$  509  $[M]^+$  (9), 491 (4), 322 (28), 321 (25), 180 (45), 167 (40), 166 (100), 165 (49), 154 (47), 138 (33); HREIMS  $m/z$  509.2467 (calcd. for  $C_{26}H_{39}NO_7S$ , 509.2447).

**Epothilone B<sub>10</sub> (9):** colorless amorphous solid;  $[\alpha]^{22}_D$   $-27$  ( $c$  0.15, MeOH); UV (MeOH)  $\lambda_{max}$  nm ( $\epsilon$ ) 212 (15800), 247 (12500); IR (KBr)  $\nu_{max}$  3434, 2962, 2930, 2876, 2858, 1733, 1692, 1461, 1259, 1052, 981  $cm^{-1}$ ;  $^1H$  NMR ( $CDCl_3$ , 600 MHz)  $\delta$  6.99 (1H, s, H-19), 6.60 (1H, bs, H-17), 5.42 (1H, dd,  $J = 8.0, 3.0$  Hz, H-15), 4.25 (1H, ddd,  $J = 9.5, 6.3, 2.8$  Hz, H-3), 4.23 (1H, bs, 3-OH), 3.77 (1H, ddd,  $J = 4.0, 3.9, 3.8$  Hz, H-7), 3.30 (1H, dq,  $J = 4.0, 6.9$  Hz, H-6), 3.01 (2H, q,  $J = 7.6$  Hz, H-21), 2.81 (1H, dd,  $J = 7.7, 4.6$  Hz, H-13), 2.68 (1H, bs, 7-OH), 2.54 (1H, dd,  $J = 13.9, 9.5$  Hz, H-2a), 2.36 (1H, dd,  $J = 13.9, 2.8$  Hz, H-2b), 2.11 (1H, ddd,  $J = 15.3, 4.6, 3.0$  Hz, H-14a), 2.09 (3H, s, H-27), 1.91 (1H, ddd,  $J = 15.3, 8.0, 7.7$  Hz, H-14b), 1.74 (1H, m, H-8), 1.73 (1H, m, H-11a), 1.51 (1H, m, H-10a), 1.41 (1H, m, H-11b), 1.39 (3H, t,  $J = 7.6$  Hz, H-28), 1.38 (3H, m, H-9 and H-10b), 1.37 (3H, s, H-23), 1.28 (3H, s, H-26), 1.17 (3H, d,  $J = 6.9$  Hz, H-24), 1.09 (3H, s, H-22), 1.01 (3H, d,  $J = 7.0$  Hz, H-25); EIMS  $m/z$  521  $[M]^+$  (22), 449 (7), 350 (18), 334 (57), 248 (16), 234 (27), 196 (41), 182 (59), 180 (96), 178 (100), 166 (44), 154 (44); HREIMS  $m/z$  521.2808 (calcd. for  $C_{28}H_{43}NO_6S$ , 521.2811).

**Epothilone G<sub>1</sub> (10):** colorless amorphous solid;  $[\alpha]^{22}_D$   $-39.7$  ( $c$  1.0, MeOH); UV (MeOH)  $\lambda_{max}$  nm ( $\epsilon$ ) 203 (15200), 236 (15100); IR (KBr)  $\nu_{max}$  3456, 2962, 2933, 2876, 1736,

1691, 1585, 1466, 1262, 980  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.47 (1H, s, H-19), 6.33 (1H, bs, H-17), 5.42 (1H, dd,  $J = 8.3, 2.9$  Hz, H-15), 4.11 (1H, ddd,  $J = 10.1, 6.1, 3.4$  Hz, H-3), 3.78 (1H, bddd,  $J = 5.2, 3.5, 3.5$  Hz, H-7), 3.63 (1H, bd,  $J = 6.1$  Hz, 3-OH), 3.21 (1H, dq,  $J = 5.2, 7.0$  Hz, H-6), 3.00 (1H, ddd,  $J = 7.7, 4.8, 4.2$  Hz, H-13), 2.88 (1H, ddd,  $J = 7.1, 4.2, 4.2$  Hz, H-12), 2.53 (1H, dd,  $J = 14.8, 10.1$  Hz, H-2a), 2.51 (1H, bd,  $J = 3.5$  Hz, 7-OH), 2.43 (1H, dd,  $J = 14.8, 3.4$  Hz, H-2b), 2.43 (3H, s, H-21), 2.07 (1H, ddd,  $J = 15.1, 4.8, 2.9$  Hz, H-14a), 1.99 (3H, d,  $J = 1.3$  Hz, H-27), 1.86 (1H, ddd,  $J = 15.1, 8.3, 7.7$  Hz, H-14b), 1.71 (1H, m, H-8), 1.69 (1H, m, H-11a), 1.53 (1H, m, H-10a), 1.42 (1H, m, H-11b), 1.40 (3H, m, H-9 and H-10b), 1.34 (3H, s, H-23), 1.16 (3H, d,  $J = 7.0$  Hz, H-24), 1.09 (3H, s, H-22), 0.99 (3H, d,  $J = 6.9$  Hz, H-25);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  220.1 (s, C-5), 170.5 (s, C-1), 161.0 (s, C-20), 137.4 (s, C-18), 136.7 (s, C-16), 135.9 (d, C-19), 116.4 (d, C-17), 76.4 (d, C-15), 74.9 (d, C-7), 73.7 (d, C-3), 57.4 (d, C-12), 54.4 (d, C-13), 52.6 (s, C-4), 43.8 (d, C-6), 38.8 (t, C-2), 36.2 (d, C-8), 31.4 (t, C-14), 30.4 (t, C-9), 27.0 (t, C-11), 23.9 (t, C-10), 21.3 (q, C-23), 21.2 (q, C-22), 17.2 (q, C-25), 15.8 (q, C-27), 14.4 (q, C-24), 13.8 (q, C-21); EIMS  $m/z$  477  $[\text{M}]^+$  (4), 405 (7), 290 (40), 152 (39), 150 (100), 148 (23), 124 (23); HREIMS  $m/z$  477.2684 (calcd. for  $\text{C}_{26}\text{H}_{39}\text{NO}_7$ , 477.2727).

**Epothilone G<sub>2</sub> (11):** colorless amorphous solid;  $[\alpha]_D^{22}$   $-22.6$  ( $c$  1.0, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) 202 (21500), 236 (14800); IR (KBr)  $\nu_{\text{max}}$  3456, 2965, 2934, 2877, 1737, 1690, 1586, 1464, 1250, 980  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.48 (1H, s, H-19), 6.33 (1H, bs, H-17), 5.43 (1H, dd,  $J = 7.1, 3.6$  Hz, H-15), 4.12 (1H, ddd,  $J = 9.9, 6.4, 3.4$  Hz, H-3), 3.77 (1H, ddd,  $J = 4.7, 4.4, 4.1$  Hz, H-7), 3.83 (1H, bd,  $J = 6.4$  Hz, 3-OH), 3.30 (1H, dq,  $J = 4.7, 6.9$

Hz, H-6), 2.78 (1H, dd,  $J = 7.0, 5.4$  Hz, H-13), 2.54 (1H, dd,  $J = 14.3, 9.9$  Hz, H-2a), 2.51 (1H, bd,  $J = 4.1$  Hz, 7-OH), 2.44 (3H, s, H-21), 2.40 (1H, dd,  $J = 14.3, 3.4$  Hz, H-2b), 2.03 (1H, ddd,  $J = 15.2, 5.4, 3.6$  Hz, H-14a), 2.00 (3H, d,  $J = 1.3$  Hz, H-27), 1.92 (1H, ddd,  $J = 15.1, 7.1, 7.0$  Hz, H-14b), 1.71 (1H, m, H-8), 1.68 (1H, m, H-11a), 1.51 (1H, m, H-10a), 1.42 (1H, m, H-11b), 1.39 (3H, m, H-9 and H-10b), 1.35 (3H, s, H-23), 1.26 (3H, s, H-26), 1.16 (3H, d,  $J = 6.9$  Hz, H-24), 1.07 (3H, s, H-22), 0.99 (3H, d,  $J = 7.0$  Hz, H-25);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  220.7 (s, C-5), 170.5 (s, C-1), 161.0 (s, C-20), 137.4 (s, C-18), 136.5 (s, C-16), 135.9 (d, C-19), 116.3 (d, C-17), 76.6 (d, C-15), 74.6 (d, C-7), 73.5 (d, C-3), 61.3 (s, C-12), 61.1 (d, C-13), 52.7 (s, C-4), 43.4 (d, C-6), 39.0 (t, C-2), 36.5 (d, C-8), 32.0 (t, C-11), 31.8 (t, C-14), 30.8 (t, C-9), 22.8 (t, C-10), 22.9 (q, C-26), 21.0 (q, C-23), 20.8 (q, C-22), 17.2 (q, C-25), 15.9 (q, C-27), 14.1 (q, C-24), 13.8 (q, C-21); EIMS  $m/z$  491 $[\text{M}]^+$  (21), 419 (6), 320 (18), 304 (39), 166 (42), 152 (57), 150 (100), 149 (44), 148 (58), 124 (35), 109 (33); HREIMS  $m/z$  491.2878 (calcd. for  $\text{C}_{27}\text{H}_{41}\text{NO}_7$ , 491.2883).

Epothilone H<sub>1</sub> (12): colorless amorphous solid;  $[\alpha]_{\text{D}}^{22} -84.2$  ( $c$  0.2, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) 203 (19600), 237 (12000); IR (KBr)  $\nu_{\text{max}}$  3436, 2933, 2880, 2860, 1734, 1688, 1585, 1251, 1007  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.47 (1H, s, H-19), 6.31 (1H, bs, H-17), 5.43 (1H, ddd,  $J = 10.6, 10.2, 4.5$  Hz, H-12), 5.36 (1H, dddd,  $J = 10.6, 9.6, 5.0, 1.3$  Hz, H-13), 5.30 (1H, dd,  $J = 9.9, 2.0$  Hz, H-15), 4.16 (1H, ddd,  $J = 11.2, 5.3, 2.8$  Hz, H-3), 3.73 (1H, ddd,  $J = 3.9, 2.5, 2.3$  Hz, H-7), 3.12 (1H, dq,  $J = 2.3, 6.9$  Hz, H-6), 2.92 (1H, d,  $J = 2.5$  Hz, 7-OH), 2.91 (1H, d,  $J = 5.3$  Hz, 7-OH), 2.66 (1H, ddd,  $J = 15.1, 9.9, 9.6$  Hz, H-14a), 2.50 (1H, dd,  $J = 15.4, 11.2$  Hz, H-2a), 2.43 (3H, s, H-21), 2.37 (1H, dd,  $J = 15.4, 2.8$  Hz, H-2b), 2.23

(1H, m, H-14b), 2.18 (1H, m, H-11a), 2.01 (1H, m, H-11b), 2.08 (3H, d,  $J = 1.3$  Hz, H-27), 1.74 (1H, m, H-8), 1.65 (1H, m, H-10a), 1.33 (1H, m, H-9a), 1.31 (3H, s, H-23), 1.19 (1H, m, H-10b), 1.18 (1H, m, H-9b), 1.17 (3H, d,  $J = 6.9$  Hz, H-24), 1.08 (3H, s, H-22), 0.99 (3H, d,  $J = 7.1$  Hz, H-25);  $^{13}\text{C}$  NMR, see Table 1; EIMS  $m/z$  461  $[\text{M}]^+$  (6), 310 (5), 274 (10), 273 (7), 171 (63), 152 (100), 148 (18), 111 (15); HREIMS  $m/z$  461.2743 (calcd. for  $\text{C}_{26}\text{H}_{39}\text{NO}_6$ , 461.2777).

**Epothilone H<sub>2</sub> (13):** colorless amorphous solid;  $[\alpha]_{\text{D}}^{22} -44.4$  ( $c$  0.25, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) 203 (14500), 236 (12200); IR (KBr)  $\nu_{\text{max}}$  3436, 2967, 2935, 2880, 1734, 1690, 1586, 1251, 1007  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.46 (1H, s, H-19), 6.30 (1H, bs, H-17), 5.23 (1H, dd,  $J = 9.8, 2.1$  Hz, H-15), 5.12 (1H, dd,  $J = 10.1, 5.3$  Hz, H-13), 4.20 (1H, ddd,  $J = 10.8, 5.7, 2.9$  Hz, H-3), 3.71 (1H, ddd,  $J = 3.8, 2.6, 2.6$  Hz, H-7), 3.14 (1H, dq,  $J = 2.6, 6.9$  Hz, H-6), 2.93 (d,  $J = 5.7$  Hz, 3-OH), 2.90 (1H, bd,  $J = 2.6$  Hz, 7-OH), 2.62 (1H, ddd,  $J = 15.1, 9.8, 9.8$  Hz, H-14a), 2.46 (1H, dd,  $J = 15.1, 10.8$  Hz, H-2a), 2.43 (3H, s, H-21), 2.32 (1H, dd,  $J = 15.1, 2.9$  Hz, H-2b), 2.29 (1H, m, H-11a), 2.19 (1H, bd,  $J = 15.1$  Hz, H-14b), 1.97 (3H, d,  $J = 1.3$  Hz, H-27), 1.87 (1H, m, H-11b), 1.73 (1H, m, H-8), 1.67 (1H, m, H-10a), 1.65 (3H, bs, H-26), 1.32 (3H, s, H-23), 1.26 (2H, m, H-9), 1.24 (1H, m, H-10b), 1.18 (3H, d,  $J = 6.9$  Hz, H-24), 1.07 (3H, s, H-22), 1.00 (3H, d,  $J = 7.0$  Hz, H-25);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  220.6 (s, C-5), 170.3 (s, C-1), 161.0 (s, C-20), 138.6 (s, C-12), 138.4 (s, C-16), 137.5 (s, C-18), 135.6 (d, C-19), 120.8 (d, C-13), 115.8 (d, C-17), 78.9 (d, C-15), 74.3 (d, C-7), 72.7 (d, C-3), 53.3 (s, C-4), 42.0 (d, C-6), 39.6 (t, C-2), 38.6 (d, C-8), 32.4 (t, C-14), 31.9 (t, C-9), 31.6 (t, C-11), 25.6 (t, C-10), 23.0 (q, C-26), 22.8 (q, C-23), 18.8 (q, C-22), 16.1 (q, C-27), 15.9 (q, C-25), 13.8 (q, C-21), 13.6 (q, C-24); EIMS  $m/z$  475  $[\text{M}]^+$  (11), 288 (9), 287 (5), 188 (7), 171 (32), 152 (100),

111 (10); HREIMS  $m/z$  475.2913 (calcd. for  $C_{27}H_{41}NO_6$ , 475.2934).

**Epothilone C<sub>1</sub> (16):** colorless amorphous solid;  $[\alpha]_D^{22}$  -114.0 (*c* 10.0, MeOH); UV (MeOH)  $\lambda_{\max}$  nm ( $\epsilon$ ) 211 (16500), 248 (12500); IR (KBr)  $\nu_{\max}$  3440, 2933, 2877, 2858, 1730, 1708, 1457, 1244, 981  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  6.96 (1H, s, H-19), 6.56 (1H, bs, H-17), 5.47 (1H, dd,  $J = 9.2, 3.0$  Hz, H-15), 5.43 (1H, m, H-12), 5.40 (1H, m, H-13), 4.40 (1H, ddd,  $J = 6.2, 6.1, 6.1$  Hz, H-3), 3.69 (1H, dd,  $J = 5.7, 3.6$  Hz, H-7), 3.01 (1H, dq,  $J = 5.7, 6.9$  Hz, H-6), 3.01 (1H, bs, 3-OH), 2.84 (1H, dq,  $J = 5.2, 7.0$  Hz, H-4), 2.68 (3H, s, H-21), 2.66 (1H, ddd,  $J = 16.4, 9.2, 7.3$  Hz, H-14a), 2.64 (1H, dd,  $J = 15.9, 7.1$  Hz, H-2a), 2.54 (1H, dd,  $J = 15.9, 6.1$  Hz, H-2b), 2.38 (1H, bd,  $J = 16.4$  Hz, H-14b), 2.35 (1H, bs, 7-OH), 2.07 (3H, bs, H-27), 2.03 (2H, m, H-11), 1.62 (1H, m, H-10a), 1.53 (1H, m, H-8), 1.35 (1H, m, H-9a), 1.22 (1H, m, H-9b), 1.19 (3H, d,  $J = 6.9$  Hz, H-24), 1.14 (3H, d,  $J = 6.9$  Hz, H-23), 1.10 (1H, m, H-10b), 0.95 (3H, d,  $J = 6.9$  Hz, H-25);  $^{13}\text{C}$  NMR, see Table 1; EIMS  $m/z$  463  $[\text{M}]^+$  (5), 324 (8), 290 (8), 204 (7), 168 (100), 164 (15), 139 (36); HREIMS  $m/z$  463.2381 (calcd. for  $\text{C}_{25}\text{H}_{37}\text{NO}_5\text{S}$ , 463.2392).

**Epothilone D<sub>1</sub> (17):** colorless amorphous solid;  $[\alpha]_D^{22}$  -118.6 (*c* 0.5, MeOH); UV (MeOH)  $\lambda_{\max}$  nm ( $\epsilon$ ) 208 (18300), 249 (11900); IR (KBr)  $\nu_{\max}$  3439, 2965, 2934, 2877, 1729, 1707, 1456, 1250, 980  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  6.98 (1H, s, H-19), 6.56 (1H, bs, H-17), 5.51 (1H, dd,  $J$  = 9.5, 3.4 Hz, H-15), 5.16 (1H, dd,  $J$  = 8.0, 4.2 Hz, H-13), 4.42 (1H, ddd,  $J$  = 7.1, 6.3, 5.5 Hz, H-3), 3.70 (1H, dd,  $J$  = 6.5, 2.9 Hz, H-7), 3.07 (1H, dq,  $J$  = 6.5, 6.9 Hz, H-6), 2.95 (1H, dq,  $J$  = 4.7, 7.0 Hz, H-4), 2.71 (3H, s, H-21), 2.69 (1H, dd,  $J$  = 16.0, 6.3 Hz, H-2a), 2.64 (1H, m, H-14a), 2.59 (1H, dd,  $J$  = 16.0, 7.1 Hz, H-2b), 2.46 (1H, bs, 3-OH), 2.38 (1H, bd,  $J$  = 16.0 Hz, H-14b), 2.19 (1H, ddd,  $J$  = 13.3, 8.6, 5.7 Hz, H-11a), 2.10 (3H, d,  $J$  = 1.4 Hz, H-27), 2.02 (1H, bs, 7-OH), 1.91 (1H, ddd,  $J$  = 13.3, 6.0, 6.0 Hz, H-11b), 1.68 (1H, m, H-10a), 1.66 (3H, bs, H-26), 1.53 (1H, m, H-8), 1.37 (1H, m, H-9a), 1.26 (1H, m, H-9b), 1.24 (3H, d,  $J$  = 6.9 Hz, H-24), 1.19 (1H, m, H-10b), 1.14 (3H, d,  $J$  = 7.0, H-23), 0.99 (3H, d,  $J$  = 6.9 Hz, H-25);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  217.0 (s, C-5), 169.7 (s, C-1), 165.0 (s, C-20), 152.2 (s, C-18), 138.5 (s, C-12), 137.7 (s, C-16), 120.7 (d, C-13), 120.1 (d, C-17), 116.3 (d, C-19), 78.8 (d, C-15), 77.2 (d, C-7), 67.7 (d, C-3), 52.1 (d, C-4), 46.5 (d, C-6), 40.6 (t, C-2), 37.6 (d, C-8), 32.3 (t, C-14), 31.8 (t, C-11), 29.5 (t, C-9), 25.5 (t, C-10), 23.1 (q, C-26), 19.2 (q, C-21), 15.5 (q, C-27), 16.6 (q, C-25), 14.5 (q, C-24), 9.7 (q, C-23); EIMS  $m/z$  477  $[\text{M}]^+$  (13), 304 (19), 303 (31), 218 (40), 204 (41), 168 (100), 164 (45), 157 (25), 139 (18); HREIMS  $m/z$  477.2544 (calcd. for  $\text{C}_{26}\text{H}_{39}\text{NO}_5\text{S}$ , 477.2549).

**Epothilone C<sub>2</sub> (18):** colorless amorphous solid;  $[\alpha]_D^{22}$  -11.6 (*c* 10.0, MeOH); UV (MeOH)  $\lambda_{\max}$  nm ( $\epsilon$ ) 212 (15500), 249 (12100); IR (KBr)  $\nu_{\max}$  3428, 2962, 2929, 2877, 2859, 1734, 1705, 1460, 1251, 982  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  6.99 (1H, s, H-19), 6.66 (1H,

bs, H-17), 5.55 (1H, ddd,  $J = 10.4, 9.2, 6.1$  Hz, H-12), 5.38 (1H, ddd,  $J = 10.4, 9.3, 6.2$  Hz, H-13), 5.22 (1H, dd,  $J = 8.8, 2.8$  Hz, H-15), 4.42 (1H, dddd,  $J = 9.4, 5.6, 4.2, 4.1$  Hz, H-3), 3.93 (1H, d,  $J = 5.6$  Hz, 3-OH), 3.86 (1H, m, H-7), 3.15 (1H, bs, 7-OH), 3.12 (1H, dq,  $J = 4.2, 7.0$  Hz, H-4), 3.00 (1H, dq,  $J = 6.9, 7.0$  Hz, H-6), 2.70 (3H, s, H-21), 2.62 (1H, dddd,  $J = 15.1, 9.3, 8.8, 0.8$  Hz, H-14a), 2.58 (1H, dd,  $J = 15.4, 9.4$  Hz, H-2a), 2.38 (1H, dd,  $J = 15.4, 4.1$  Hz, H-2b), 2.31 (1H, ddd,  $J = 15.1, 6.2, 2.8$  Hz, H-14b), 2.08 (3H, d,  $J = 1.3$  Hz, H-27), 2.15 (1H, m, H-11a), 2.04 (1H, m, H-11b), 1.71 (1H, m, H-8), 1.59 (1H, m, H-10a), 1.43 (1H, m, H-9a), 1.31 (1H, m, H-9b), 1.26 (3H, d,  $J = 7.0$  Hz, H-24), 1.15 (3H, d,  $J = 7.0$  Hz, H-23), 1.11 (1H, m, H-10b), 1.00 (3H, d,  $J = 6.9$  Hz, H-25);  $^{13}\text{C}$  NMR, see Table 1; EIMS  $m/z$  463  $[\text{M}]^+$  (7), 324 (7), 306 (8), 290 (17), 168 (100), 164 (14), 139 (27); HREIMS  $m/z$  463.2392 (calcd. for  $\text{C}_{25}\text{H}_{37}\text{NO}_5\text{S}$ , 463.2392).

**Epothilone D<sub>2</sub> (19):** colorless amorphous solid;  $[\alpha]_{\text{D}}^{22} -12.5$  ( $c$  1.0, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) 210 (15400), 248 (11200); IR (KBr)  $\nu_{\text{max}}$  3436, 2965, 2930, 2877, 1732, 1705, 1458, 1253, 980  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  6.97 (1H, s, H-19), 6.56 (1H, bs, H-17), 5.18 (1H, dd,  $J = 7.9, 4.9$  Hz, H-15), 5.18 (1H, ddd,  $J = 9.6, 5.4, 1.0$  Hz, H-13), 4.27 (1H, m, H-3), 3.88 (1H, dd,  $J = 5.6, 4.6$  Hz, H-7), 3.19 (1H, bs, 3-OH), 3.07 (1H, dq,  $J = 4.3, 7.0$  Hz, H-4), 2.95 (1H, dq,  $J = 5.6, 7.0$  Hz, H-6), 2.70 (3H, s, H-21), 2.62 (1H, dd,  $J = 14.9, 7.8$  Hz, H-2a), 2.56 (1H, ddd,  $J = 14.7, 9.6, 7.9$  Hz, H-14a), 2.43 (1H, dd,  $J = 14.9, 5.6$  Hz, H-2b), 2.38 (1H, bs, 7-OH), 2.26 (1H, ddd,  $J = 14.5, 5.4, 4.9$  Hz, H-14b), 2.19 (1H, ddd,  $J = 13.0, 10.4, 5.4$  Hz, H-11a), 2.10 (3H, d,  $J = 1.4$  Hz, H-27), 1.95 (1H, ddd,  $J = 13.0, 10.3, 5.3$  Hz, H-11b), 1.72 (1H, m, H-8), 1.68 (3H, bs, H-26), 1.61 (1H, m, H-10a), 1.39 (2H, m, H-9), 1.21 (1H, m, H-10b).



1.19 (3H, d,  $J = 6.9$  Hz, H-24), 1.17 (3H, d,  $J = 7.0$ , H-22), 1.00 (3H, d,  $J = 6.9$  Hz, H-25);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  216.8 (s, C-5), 170.4 (s, C-1), 164.9 (s, C-20), 152.3 (s, C-18), 139.8 (s, C-12), 137.5 (s, C-16), 120.5 (d, C-17), 119.2 (d, C-13), 116.3 (d, C-19), 80.0 (d, C-15), 74.3 (d, C-7), 69.7 (d, C-3), 48.6 (d, C-4), 48.4 (d, C-6), 39.9 (t, C-2), 36.6 (d, C-8), 32.2 (t, C-14), 32.7 (t, C-11), 30.9 (t, C-9), 26.0 (t, C-10), 23.6 (q, C-26), 19.2 (q, C-21), 15.4 (q, C-27), 17.1 (q, C-25), 12.4 (q, C-24), 12.7 (q, C-23); EIMS  $m/z$  477  $[\text{M}]^+$  (22), 304 (19), 303 (17), 218 (22), 204 (25), 168 (100), 164 (28), 157 (31), 139 (21); HREIMS  $m/z$  477.2545 (calcd. for  $\text{C}_{26}\text{H}_{39}\text{NO}_5\text{S}$ , 477.2549).

**Epothilone C<sub>3</sub> (20):** colorless amorphous solid;  $[\alpha]_D^{22} -62.1$  ( $c$  5.0, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) 212 (16200), 248 (12300); IR (KBr)  $\nu_{\text{max}}$  3432, 2928, 2878, 2858, 1736, 1698, 1252, 1040  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  6.95 (1H, s, H-19), 6.56 (1H, bs, H-17), 5.44 (1H, ddd,  $J = 10.9, 10.3, 5.4$  Hz, H-12), 5.33 (1H, ddd,  $J = 10.9, 9.3, 4.6$  Hz, H-13), 5.23 (1H, dd,  $J = 9.5, 2.2$  Hz, H-15), 4.36 (1H, ddd,  $J = 11.3, 5.6, 2.3$  Hz, H-3), 4.04 (1H, d,  $J = 5.6$  Hz, 3-OH), 3.93 (1H, ddd,  $J = 9.5, 2.3, 1.4$  Hz, H-7), 3.56 (1H, bd,  $J = 2.3$  Hz, 7-OH), 2.70 (1H, dd,  $J = 18.0, 1.4$  Hz, H-6a), 2.67 (3H, s, H-21), 2.61 (1H, ddd,  $J = 15.3, 9.5, 9.3$  Hz, H-14a), 2.38 (1H, dd,  $J = 14.3, 11.3$  Hz, H-2a), 2.36 (1H, dd,  $J = 18.0, 9.5$  Hz, H-6b), 2.28 (1H, bd,  $J = 15.3$  Hz, H-14b), 2.12 (1H, m, H-11a), 2.06 (1H, dd,  $J = 14.3, 2.3$  Hz, H-2b), 2.03 (3H, d,  $J = 1.3$  Hz, H-27), 1.96 (1H, m, H-11b), 1.75 (1H, m, H-8), 1.54 (1H, m, H-10a), 1.26 (1H, m, H-9a), 1.25 (3H, s, H-23), 1.17 (1H, m, H-10b), 1.15 (1H, m, H-9b), 1.03 (3H, s, H-22), 0.91 (3H, d,  $J = 6.8$  Hz, H-25);  $^{13}\text{C}$  NMR, see Table 1; EIMS  $m/z$  463  $[\text{M}]^+$  (28), 290 (14), 168 (100), 164 (36), 157 (44), 151 (25); HREIMS  $m/z$  463.2379 (calcd. for  $\text{C}_{25}\text{H}_{37}\text{NO}_5\text{S}$ , 463.2392).

**Epothilone C<sub>4</sub> (21):** colorless amorphous solid;  $[\alpha]_D^{22} -75.6$  (*c* 1.0, MeOH); UV (MeOH)  $\lambda_{\max}$  nm ( $\epsilon$ ) 212 (17200), 248 (12500); IR (KBr)  $\nu_{\max}$  3434, 2974, 2932, 2859, 1735, 1686, 1252, 1046  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  6.96 (1H, s, H-19), 6.60 (1H, bs, H-17), 5.43 (1H, m, H-12), 5.40 (1H, m, H-13), 5.26 (1H, dd,  $J = 9.6, 2.3$  Hz, H-15), 4.41 (1H, ddd,  $J = 11.4, 5.8, 2.5$  Hz, H-3), 3.78 (1H, m, H-7), 3.70 (1H, bs, 3-OH), 3.46 (1H, d,  $J = 0.9$  Hz, 7-OH), 3.01 (1H, dq,  $J = 0.5, 7.0$  Hz, H-6), 2.69 (3H, s, H-21), 2.66 (1H, ddd,  $J = 15.3, 9.6, 8.8$  Hz, H-14a), 2.47 (1H, dd,  $J = 14.5, 11.4$  Hz, H-2a), 2.29 (1H, m, H-14b), 2.25 (1H, dd,  $J = 14.5, 2.5$  Hz, H-2b), 2.24 (1H, m, H-11a), 2.07 (3H, d,  $J = 1.4$  Hz, H-27), 1.96 (1H, m, H-11b), 1.51 (2H, m, H-8), 1.44 (2H, m, H-10), 1.37 (2H, m, H-9), 1.32 (3H, s, H-23), 1.17 (3H, d,  $J = 7.0$  Hz, H-24), 1.07 (3H, s, H-22);  $^{13}\text{C}$  NMR, see Table 1; EIMS  $m/z$  463  $[\text{M}]^+$  (7), 276 (15), 171 (33), 168 (100), 164 (23), 151 (22), 111 (13); HREIMS  $m/z$  463.2373 (calcd. for  $\text{C}_{25}\text{H}_{37}\text{NO}_5\text{S}$ , 463.2392).

**Epothilone C<sub>5</sub> (22):** colorless amorphous solid;  $[\alpha]_D^{22} -158.2$  (*c* 0.5, MeOH); UV (MeOH)  $\lambda_{\max}$  nm ( $\epsilon$ ) 205 (19500), 247 (12700); IR (KBr)  $\nu_{\max}$  3447, 2972, 2927, 1737, 1690, 1450, 1252, 1181, 986  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  6.93 (1H, s, H-19), 6.48 (1H, bs, H-17), 5.48 (1H, ddd,  $J = 10.7, 6.2, 6.2$  Hz, H-12), 5.39 (1H, m, H-13), 5.37 (1H, m, H-9), 5.34 (1H, dd,  $J = 8.0, 2.3$  Hz, H-15), 4.29 (1H, dd,  $J = 6.0, 2.6$  Hz, H-7), 4.09 (1H, ddd,  $J = 10.8, 7.1, 2.9$  Hz, H-3), 3.59 (1H, d,  $J = 7.1$  Hz, 3-OH), 3.17 (1H, dq,  $J = 6.0, 6.9$  Hz, H-6), 2.68 (3H, s, H-21), 2.54 (1H, ddd,  $J = 15.2, 8.1, 8.0$  Hz, H-14a), 2.44 (1H, bs, 7-OH), 2.42 (1H, dd,  $J = 15.1, 2.9$  Hz, H-2a), 2.41 (1H, ddd,  $J = 15.2, 2.3, 2.3$  Hz, H-14b), 2.34 (1H, dd,  $J = 15.1, 10.8$  Hz, H-2b), 2.20 (1H, m, H-10a), 2.18 (2H, m, H-11), 2.12 (1H, m, H-10b), 2.06 (3H, bs, H-27), 1.67 (3H, bs, H-25), 1.27 (3H, s, H-23), 1.21 (3H, d,  $J = 6.9$  Hz, H-24), 1.15 (3H, s, H-22);  $^{13}\text{C}$  NMR,

see Table 1; EIMS  $m/z$  475  $[M]^+$  (6), 392 (7), 304 (6), 288 (33), 204 (76), 171 (19), 168 (100), 164 (12); HREIMS  $m/z$  475.2380 (calcd. for  $C_{26}H_{37}NO_5S$ , 475.2392).

**Epothilone D<sub>5</sub> (23):** colorless amorphous solid;  $[\alpha]_D^{22} -150$  ( $c$  0.2, MeOH); UV (MeOH)  $\lambda_{max}$  nm ( $\epsilon$ ) 205 (23300), 248 (13600); IR (KBr)  $\nu_{max}$  3439, 2967, 2927, 1736, 1690, 1451, 1254, 1181, 987  $cm^{-1}$ ;  $^1H$  NMR ( $CDCl_3$ , 400 MHz)  $\delta$ : 6.94 (1H, s, H-19), 6.51 (1H, bs, H-17), 5.34 (1H, bs, H-9), 5.29 (1H, dd,  $J = 8.0, 2.4$  Hz, H-15), 5.16 (1H, dd,  $J = 8.2, 6.2$  Hz, H-13), 4.30 (1H, bd,  $J = 4.9$  Hz, H-7), 4.19 (1H, ddd,  $J = 10.8, 7.6, 3.0$  Hz, H-3), 3.68 (1H, d,  $J = 7.6$  Hz, 3-OH), 3.17 (1H, dq,  $J = 4.9, 7.0$  Hz, H-6), 2.69 (3H, s, H-21), 2.65 (1H, d,  $J = 2.1$  Hz, 7-OH), 2.56 (1H, ddd,  $J = 16.2, 8.2, 8.0$  Hz, H-14a), 2.40 (1H, dd,  $J = 15.0, 3.0$  Hz, H-2a), 2.39 (1H, bd,  $J = 16.2$  Hz, H-14b), 2.34 (1H, dd,  $J = 15.0, 10.8$  Hz, H-2b), 2.25 (2H, m, H-10a and H-11a), 2.20 (1H, m, H-10b), 2.17 (1H, m, H-11b), 2.05 (3H, d,  $J = 1.0$  Hz, H-27), 1.69 (3H, bs, H-25), 1.68 (3H, bs, H-26), 1.29 (3H, s, H-23), 1.23 (3H, d,  $J = 7.0$  Hz, H-24), 1.16 (3H, s, H-22);  $^{13}C$  NMR, see Table 1; EIMS  $m/z$  489  $[M]^+$  (4), 406 (4), 338 (7), 302 (13), 218 (35), 171 (10), 168 (100), 153 (20), 125 (10); HREIMS  $m/z$  489.2536 (calcd. for  $C_{27}H_{39}NO_5S$ , 489.2549).

**Epothilone C<sub>6</sub> (24):** colorless amorphous solid;  $[\alpha]_D^{22} -205.2$  ( $c$  1.0, MeOH); UV (MeOH)  $\lambda_{max}$  nm ( $\epsilon$ ) 218 (24600), 237 (28800); IR (KBr)  $\nu_{max}$  3435, 2967, 2927, 2882, 1732, 1688, 1465, 1258, 988  $cm^{-1}$ ;  $^1H$  NMR ( $CDCl_3$ , 300 MHz)  $\delta$ : 6.97 (1H, s, H-19), 6.58 (1H, bs, H-17), 6.43 (1H, dd, 15.5, 10.8 Hz, H-11), 6.11 (1H, dd,  $J = 10.8, 10.6$  Hz, H-12), 5.75 (1H, ddd,  $J = 15.5, 8.3, 5.6$  Hz, H-10), 5.34 (1H, m, H-13), 5.34 (1H, dd,  $J = 9.7, 2.4$  Hz, H-15), 4.16 (1H, ddd,  $J = 9.2, 4.9, 4.3$  Hz, H-3), 3.74 (1H, ddd,  $J = 2.2, 2.1, 1.7$  Hz, H-7), 3.24 (1H, dq,  $J = 2.1, 6.9$  Hz, H-6), 3.06 (1H, d,  $J = 2.2$  Hz, 7-OH), 2.93 (1H, d,  $J = 4.9$  Hz, 3-OH), 2.78 (1H, dddd,

$J = 14.1$ , 9.9 9.7, 0.7, H-14a), 2.71 (3H, s, H-21), 2.48 (1H, m, H-9a), 2.47 (1H, dd,  $J = 15.5$ , 9.2 Hz, H-2a), 2.40 (1H, dd,  $J = 15.5$ , 4.3 Hz, H-2b), 2.38 (1H, bdd,  $J = 14.1$ , 7.8 Hz, H-14b), 2.11 (3H, d,  $J = 1.3$  Hz, H-27), 1.96 (1H, m, H-8), 1.33 (3H, s, H-23), 1.11 (3H, d,  $J = 6.9$  Hz, H-24), 1.06 (3H, s, H-22), 1.05 (3H, d,  $J = 6.8$  Hz, H-25);  $^{13}\text{C}$  NMR, see Table 1; EIMS  $m/z$  475  $[\text{M}]^+$  (13), 387 (2), 316 (4), 288 (15), 230 (16), 204 (9), 171 (18), 168 (100), 164 (14), 151 (17); HREIMS  $m/z$  475.2361 (calcd. for  $\text{C}_{26}\text{H}_{37}\text{NO}_5\text{S}$ , 475.2392).

Epothilone C<sub>7</sub> (25): colorless amorphous solid;  $[\alpha]_{\text{D}}^{22}$  -XXX (*c* 2.0, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) XXX (XXX), XXX (XXX); IR (KBr)  $\nu_{\text{max}}$  XXX  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.01 (1H, s, H-19), 6.66 (1H, bs, H-17), 5.59 (1H, ddd,  $J = 11.1$ , 11.1, 3.8 Hz, H-12), 5.40 (1H, dd,  $J = 11.1$ , 9.2, H-13), 5.03 (1H, d,  $J = 9.3$  Hz, H-15), 4.62 (1H, dd,  $J = 9.3$ , 9.2 Hz, H-14), 4.18 (1H, bd,  $J = 11.0$  Hz, H-3), 3.72 (1H, bs, H-7), 3.20 (1H, bs, 3-OH), 3.09 (1H, dq,  $J = 1.9$ , 6.8 Hz, H-6), 3.00 (1H, bs, 7-OH), 2.69 (3H, s, H-21), 2.47 (1H, dd,  $J = 14.8$ , 11.0 Hz, H-2a), 2.32 (1H, dd,  $J = 14.8$ , 2.6 Hz, H-2b), 2.27 (1H, m, H-11a), 2.19 (3H, bs, H-27), 2.13 (1H, m, H-11b), 1.76 (1H, m, H-8), 1.70 (1H, m, H-10a), 1.35 (1H, m, H-9a), 1.32 (3H, s, H-23), 1.23 (1H, m, H-9b), 1.21 (1H, m, H-10b), 1.18 (3H, d,  $J = 6.8$  Hz, H-24), 1.08 (3H, s, H-22), 1.00 (3H, d,  $J = 6.9$  Hz, H-25); EIMS  $m/z$  493  $[\text{M}]^+$  XXX; HREIMS  $m/z$  493.XXX (calcd. for  $\text{C}_{26}\text{H}_{39}\text{NO}_6\text{S}$ , 493.2498).

Epothilone C<sub>8</sub> (26): colorless amorphous solid;  $[\alpha]_{\text{D}}^{22}$  -75.2 (*c* 2.5, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) 210 (16800), 248 (17800); IR (KBr)  $\nu_{\text{max}}$  3443, 2932, 2881, 1734, 1689, 1465, 1255, 1183, 976  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  6.93 (1H, s, H-19), 6.62 (1H, dd,  $J = 15.6$ , 0.6 Hz, H-17), 6.49 (1H, dd,  $J = 15.6$ , 6.6 Hz, H-16), 5.52 (1H, dddd,  $J = 9.5$ , 6.6, 2.8, 0.6 Hz, H-

15), 5.42 (1H, m, H-12), 5.41 (1H, m, H-13), 4.13 (1H, ddd,  $J = 11.0, 5.3, 2.8$  Hz, H-3), 3.69 (1H, ddd,  $J = 3.7, 2.8, 2.5$  Hz, H-7), 3.11 (1H, dq,  $J = 2.5, 6.8$  Hz, H-6), 2.95 (1H, d,  $J = 5.3$  Hz, 3-OH), 2.90 (1H, d,  $J = 2.8$  Hz, 7-OH), 2.69 (3H, s, H-21), 2.67 (1H, ddd,  $J = 14.9, 9.5, 8.4$  Hz, H-14a), 2.48 (1H, dd,  $J = 15.6, 11.0$  Hz, H-2a), 2.33 (1H, dd,  $J = 15.6, 2.8$  Hz, H-2b), 2.30 (1H, bd,  $J = 14.9$  Hz, H-14b), 2.14 (1H, m, H-11a), 2.03 (1H, m, H-11b), 1.71 (1H, m, H-8), 1.63 (1H, m, H-10a), 1.31 (1H, m, H-9a), 1.29 (3H, s, H-23), 1.17 (3H, d,  $J = 6.8$  Hz, H-24), 1.16 (1H, m, H-10b), 1.14 (1H, m, H-9b), 1.05 (3H, s, H-22), 0.97 (3H, d,  $J = 7.1$  Hz, H-25);  $^{13}\text{C}$  NMR, see Table 1; EIMS  $m/z$  463  $[\text{M}]^+$  (21), 310 (10), 276 (21), 171 (83), 154 (100), 150 (27), 111 (18); HREIMS  $m/z$  463.2382 (calcd. for  $\text{C}_{25}\text{H}_{37}\text{NO}_5\text{S}$ , 463.2392).

**Epothilone C<sub>9</sub> (27):** colorless amorphous solid;  $[\alpha]_D^{22} -93.4$  ( $c$  1.0, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) 209 (15200), 254 (15700); IR (KBr)  $\nu_{\text{max}}$  3416, 2966, 2932, 1736, 1689, 1463, 1249, 1011  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.06 (1H, s, H-19), 6.65 (1H, bs, H-17), 6.56 (1H, dd,  $J = 10.6, 4.4$  Hz, 27-OH), 5.55 (1H, d,  $J = 6.2$  Hz, 3-OH), 5.52 (1H, dd,  $J = 11.6, 2.0$  Hz, H-15), 5.44 (1H, dddd,  $J = 11.2, 10.7, 3.1, 1.7$  Hz, H-12), 5.35 (1H, dddd,  $J = 11.0, 10.7, 3.9, 1.7$  Hz, H-13), 4.47 (1H, ddd,  $J = 12.5, 4.4, 1.3$  Hz, H-27a), 4.35 (1H, ddd,  $J = 11.7, 6.2, 2.6$  Hz, H-3), 4.20 (1H, ddd,  $J = 12.5, 10.6, 0.9$  Hz, H-27b), 3.63 (1H, ddd,  $J = 4.6, 1.8, 0.9$  Hz, H-7), 3.24 (1H, d,  $J = 1.8$  Hz, 7-OH), 3.13 (1H, dq,  $J = 0.9, 6.8$  Hz, H-6), 2.80 (1H, ddd,  $J = 14.8, 11.6, 11.0$  Hz, H-14a), 2.71 (3H, s, H-21), 2.40 (1H, dd,  $J = 14.4, 11.7$  Hz, H-2a), 2.24 (1H, m, H-11a), 2.06 (1H, dd,  $J = 14.4, 2.6$  Hz, H-2b), 2.01 (1H, ddd,  $J = 14.8, 3.9, 2.0$  Hz, H-14b), 2.00 (1H, m, H-11b), 1.77 (1H, m, H-8), 1.69 (1H, m, H-10a), 1.35 (1H, m, H-9a), 1.35 (3H, s, H-23), 1.19 (1H, m, H-10b), 1.19 (3H, d,  $J = 6.8$  Hz, H-24), 1.18 (1H, m, H-9b), 1.01 (3H, d,  $J =$

7.1 Hz, H-25), 0.98 (3H, s, H-22);  $^{13}\text{C}$  NMR, see Table 1; EIMS  $m/z$  493  $[\text{M}]^+$  (17), 306 (64), 184 (50), 171 (30), 167 (38), 166 (100), 138 (12); HREIMS  $m/z$  493.2502 (calcd. for  $\text{C}_{26}\text{H}_{39}\text{NO}_6\text{S}$ , 493.2498).

**trans-Epothilone C<sub>1</sub> (28):** colorless amorphous solid;  $[\alpha]_{\text{D}}^{22} -84$  ( $c$  0.2, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) 211 (17400), 248 (12900); IR (KBr)  $\nu_{\text{max}}$  3433, 2961, 2933, 2879, 1730, 1708, 1457, 1251, 975  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 600 MHz)  $\delta$  7.00 (1H, s, H-19), 6.64 (1H, bs, H-17), 5.45 (1H, ddd,  $J = 15.2, 6.5, 6.5$  Hz, H-12), 5.42 (1H, dd,  $J = 6.4, 3.7$  Hz, H-15), 5.35 (1H, dt,  $J = 15.2, 7.1$  Hz, H-13), 4.42 (1H, m, H-3), 3.58 (1H, ddd,  $J = 8.1, 7.9, 2.8$  Hz, H-7), 3.24 (1H, m, H-6), 3.14 (1H, dq,  $J = 4.0, 6.9$  Hz, H-6), 2.92 (1H, d,  $J = 7.9$  Hz, 7-OH), 2.71 (3H, s, H-21), 2.71 (2H, m, H-2), 2.53 (2H, m, H-14), 2.17 (1H, d,  $J = 2.17$  Hz, 3-OH), 2.11 (1H, m, H-11a), 2.06 (3H, bs, H-27), 1.93 (1H, m, H-11b), 1.68 (1H, m, H-9a), 1.65 (1H, m, H-10a), 1.33 (1H, m, H-8), 1.26 (3H, d,  $J = 6.8$  Hz, H-24), 1.16 (1H, m, H-10b), 1.12 (3H, d,  $J = 6.9$  Hz, H-22), 1.07 (1H, m, H-9b), 1.00 (3H, d,  $J = 6.8$  Hz, H-25);  $^{13}\text{C}$  NMR, see Table 1; EIMS  $m/z$  463  $[\text{M}]^+$  (6), 290 (21), 289 (20), 204 (23), 194 (19), 190 (22), 168 (100), 164 (48), 157 (14), 152 (19), 151 (17), 139 (15), 111 (18); HREIMS  $m/z$  463.2371 (calcd. for  $\text{C}_{25}\text{H}_{37}\text{NO}_5\text{S}$ , 463.2392).

**trans-Epothilone C<sub>2</sub> (29):** colorless amorphous solid;  $[\alpha]_{\text{D}}^{22} -3$  ( $c$  1.5, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) 211 (15800), 248 (11900); IR (KBr)  $\nu_{\text{max}}$  3435, 2963, 2931, 2878, 1731, 1706, 1457, 1273, 979  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 600 MHz)  $\delta$  6.99 (1H, s, H-19), 6.57 (1H, bs, H-17), 5.56 (1H, ddd,  $J = 15.1, 7.4, 7.0$  Hz, H-12), 5.41 (1H, ddd,  $J = 15.1, 7.0, 6.9$  Hz, H-13), 5.41 (1H, dd,  $J = 7.7, 2.8$  Hz, H-15), 4.13 (1H, dddd,  $J = 6.7, 6.2, 5.6, 5.1$  Hz, H-3), 3.78 (1H, ddd,  $J = 8.2, 6.5, 1.9$  Hz, H-7), 3.18 (1H, d,  $J = 5.6$  Hz, 3-OH), 3.06 (1H, dq,  $J = 8.2, 7.1$  Hz,

H-6), 2.98 (1H, dq,  $J = 6.2, 7.0$  Hz, H-4), 2.71 (3H, s, H-21), 2.64 (1H, dd,  $J = 15.1, 6.7$  Hz, H-2a), 2.54 (1H, dd,  $J = 15.1, 5.1$  Hz, H-2b), 2.44 (2H, m, H-14), 2.22 (1H, dddd,  $J = 13.8, 7.0, 6.2, 2.9$  Hz, H-11a), 2.10 (3H, d,  $J = 1.1$  Hz, H-27), 2.09 (1H, d,  $J = 6.5$  Hz, 7-OH), 1.88 (1H, dddd,  $J = 13.8, 10.9, 7.4, 2.9$  Hz, H-11b), 1.65 (1H, m, H-8), 1.63 (1H, m, H-10a), 1.56 (1H, dddd,  $J = 12.7, 12.7, 3.9, 3.9$  Hz, H-9a), 1.20 (3H, d,  $J = 7.1$  Hz, H-24), 1.15 (3H, d,  $J = 7.0$  Hz, H-23), 1.13 (1H, m, H-10b), 1.04 (1H, m, H-9b), 1.01 (3H, d,  $J = 7.0$  Hz, H-25);  $^{13}\text{C}$  NMR, see Table 1; EIMS  $m/z$  463  $[\text{M}]^+$  (13), 290 (11), 190 (10), 168 (100), 164 (20), 157 (26), 139 (17); HREIMS  $m/z$  463.2383 (calcd. for  $\text{C}_{25}\text{H}_{37}\text{NO}_5\text{S}$ , 463.2392).

**Epothilone I<sub>1</sub> (30):** colorless amorphous solid;  $[\alpha]_{\text{D}}^{22}$  -XXX (*c* XXX, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) XXX; IR (KBr)  $\nu_{\text{max}}$  XXX  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  6.96 (1H, s, H-19), 6.54 (1H, bs, H-17), 5.49 (1H, ddd,  $J = 10.3, 7.3, 7.3$  Hz, H-12), 5.33 (1H, dd,  $J = 8.3, 4.4$  Hz, H-15), 5.31 (1H, m, H-13), 4.15 (1H, ddd,  $J = 8.0, 5.0, 4.6$  Hz, H-3), 3.80 (1H, m, H-7), 3.21 (1H, dq,  $J = 6.0, 6.9$  Hz, H-6), 2.89 (1H, d,  $J = 5.0$  Hz, 3-OH), 2.70 (3H, s, H-21), 2.65 (1H, ddd,  $J = 15.8, 8.5, 8.3$  Hz, H-14a), 2.42 (2H, m, H-2), 2.35 (1H, m, H-14b), 2.27 (1H, bd,  $J = 3.3$  Hz, 7-OH), 2.13 (1H, m, H-11a), 2.09 (3H, d,  $J = 1.2$  Hz, H-27), 2.00 (1H, m, H-11b), 1.72 (1H, m, H-8), 1.40 (2H, m, H-10 $_{\beta}$ ), 1.37 (1H, m, H-9 $_{\beta}$ a), 1.36 (2H, m, H-9 $_{\alpha}$ ), 1.32 (3H, s, H-23), 1.27 (3H, m, H-9 $_{\beta}$ b and H-10 $_{\alpha}$ ), 1.13 (3H, d,  $J = 6.9$  Hz, H-24), 1.09 (3H, s, H-22), 0.94 (3H, d,  $J = 6.9$  Hz, H-25);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  221.3 (s, C-5), 171.1 (s, C-1), 164.8 (s, C-20), 152.4 (s, C-18), 137.4 (s, C-16), 133.8 (d, C-12), 124.6 (d, C-13), 120.0 (d, C-17), 116.2 (d, C-19), 78.8 (d, C-15), 74.9 (d, C-7), 74.7 (d, C-3), 51.6 (s, C-4), 43.7 (d, C-6), 38.9 (t, C-2), 34.3 (d, C-8), 31.6 (t, C-14), 29.3 (t, C-9 $_{\alpha}$ ), 28.6 (t, C-10 $_{\beta}$ ), 28.2 (t, C-10 $_{\alpha}$ ), 26.6 (t, C-

11), 24.8 (t, C-9<sub>β</sub>), 23.6 (q, C-22), 19.3 (q, C-23), 19.3 (q, C-21), 16.5 (q, C-25), 15.5 (q, C-27), 13.7 (q, C-24); EIMS  $m/z$  505 [M]<sup>+</sup> XXX; HREIMS  $m/z$  505.XXX (calcd. for C<sub>28</sub>H<sub>43</sub>NO<sub>5</sub>S, 505.XXX).

**Epothilone I<sub>2</sub> (31):** colorless amorphous solid;  $[\alpha]_D^{22}$  -XXX (c XXX, MeOH); UV (MeOH)  $\lambda_{\max}$  nm (ε) XXX; IR (KBr)  $\nu_{\max}$  XXX cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ 6.95 (1H, s, H-19), 6.53 (1H, bs, H-17), 5.40 (1H, m, H-12), 5.38 (1H, dd,  $J$  = 9.8, 3.3 Hz, H-15), 5.37 (1H, m, H-13), 4.21 (1H, ddd,  $J$  = 8.6, 3.8, 3.6 Hz, H-3), 3.85 (1H, ddd,  $J$  = 8.5, 5.8, 2.2 Hz, H-7), 3.18 (1H, dq,  $J$  = 8.5, 7.0 Hz, H-6), 2.70 (3H, s, H-21), 2.65 (1H, ddd,  $J$  = 15.2, 9.8, 9.0 Hz, H-14a), 2.51 (1H, d,  $J$  = 3.6 Hz, 3-OH), 2.37 (2H, m, H-2), 2.32 (1H, bd,  $J$  = 15.2 Hz, H-14b), 2.09 (3H, d,  $J$  = 1.3 Hz, H-27), 2.07 (2H, m, H-11), 1.78 (1H, m, H-8), 1.65 (1H, d,  $J$  = 5.8 Hz, 7-OH), 1.57 (1H, m, H-10<sub>βa</sub>), 1.44 (1H, m, H-10<sub>αa</sub>), 1.42 (1H, m, H-9<sub>β</sub>), 1.32 (3H, s, H-23), 1.21 (1H, m, H-10<sub>βb</sub>), 1.17 (3H, d,  $J$  = 7.0 Hz, H-24), 1.13 (2H, m, H-9<sub>α</sub>), 1.06 (3H, s, H-22), 0.95 (3H, d,  $J$  = 7.0 Hz, H-25<sub>α</sub>), 0.91 (3H, d,  $J$  = 6.5 Hz, H-25<sub>β</sub>), 0.68 (1H, m, H-10<sub>αb</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ 220.4 (s, C-5), 171.3 (s, C-1), XXX (s, C-20), 152.4 (s, C-18), 137.6 (s, C-16), 134.5 (d, C-12), 125.3 (d, C-13), 119.6 (d, C-17), 116.2 (d, C-19), 78.6 (d, C-15), 77.2 (d, C-7), 75.0 (d, C-3), 51.0 (s, C-4), 44.6 (d, C-6), 38.2 (t, C-2), 36.9 (t, C-9<sub>ω</sub>), 34.5 (t, C-10<sub>ω</sub>), 32.6 (d, C-8), 32.0 (t, C-14), 30.0 (d, C-9<sub>β</sub>), 27.4 (t, C-11), 26.6 (t, C-10<sub>β</sub>), 25.0 (q, C-22), 21.5 (q, C-25<sub>β</sub>), 19.3 (q, C-21), 17.9 (q, C-25<sub>ω</sub>), 17.7 (q, C-23), 15.8 (q, C-24), 15.6 (q, C-27); EIMS  $m/z$  519 [M]<sup>+</sup> XXX; HREIMS  $m/z$  519.XXX (calcd. for C<sub>29</sub>H<sub>45</sub>NO<sub>5</sub>S, 519.XXX).

**Epothilone I<sub>3</sub> (32):** colorless amorphous solid;  $[\alpha]_D^{22}$  -XXX (c XXX, MeOH); UV (MeOH)  $\lambda_{\max}$  nm (ε) XXX; IR (KBr)  $\nu_{\max}$  XXX cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 6.95 (1H,



s, H-19), 6.52 (1H, bs, H-17), 5.32 (1H, dd,  $J = 9.1, 3.0$  Hz, H-15), 5.08 (1H, dd,  $J = 8.5, 3.9$  Hz, H-13), 4.13 (1H, ddd,  $J = 9.4, 4.3, 3.2$  Hz, H-3), 3.81 (1H, m, H-7), 3.18 (1H, dq,  $J = 6.8, 7.0$  Hz, H-6), 2.83 (1H, d,  $J = 4.3$  Hz, 3-OH), 2.70 (3H, s, H-21), 2.61 (1H, ddd,  $J = 15.8, 9.1, 8.5$  Hz, H-14a), 2.43 (1H, dd,  $J = 14.0, 3.2$  Hz, H-2a), 2.38 (2H, dd,  $J = 14.0, 9.4$  Hz, H-2b), 2.30 (1H, bd,  $J = 15.8$  Hz, H-14b), 2.16 (1H, ddd,  $J = 14.1, 8.3, 7.4$  Hz, H-11a), 2.08 (3H, d,  $J = 1.0$  Hz, H-27), 1.99 (1H, d,  $J = 4.7$  Hz, 7-OH), 1.92 (1H, ddd,  $J = 14.1, 6.3, 6.3$  Hz, H-11b), 1.82 (1H, m, H-8), 1.67 (3H, s, H-26), 1.51 (1H, m, H-10<sub>β</sub>a), 1.40 (1H, m, H-9<sub>β</sub>), 1.33 (1H, m, H-10<sub>β</sub>b), 1.31 (3H, s, H-23), 1.27 (1H, m, H-10<sub>α</sub>a), 1.23 (1H, m, H-9<sub>α</sub>a), 1.16 (3H, d,  $J = 7.0$  Hz, H-24), 1.10 (1H, m, H-9<sub>α</sub>b), 1.07 (3H, s, H-22), 0.95 (3H, d,  $J = 7.0$  Hz, H-25<sub>α</sub>), 0.92 (3H, d,  $J = 6.5$  Hz, H-25<sub>β</sub>), 0.75 (1H, m, H-10<sub>α</sub>b); EIMS  $m/z$  533 [M]<sup>+</sup> XXX; HREIMS  $m/z$  533.XXX (calcd. for C<sub>30</sub>H<sub>47</sub>NO<sub>5</sub>S, 533.XXX).

Epithilone I<sub>4</sub> (33): colorless amorphous solid;  $[\alpha]_D^{22}$  -XXX (c XXX, MeOH); UV (MeOH)  $\lambda_{\max}$  nm (ε) XXX; IR (KBr)  $\nu_{\max}$  XXX cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  6.95 (1H, s, H-19), 6.53 (1H, bs, H-17), 5.47 (1H, dt,  $J = 11.1, 5.8$  Hz, H-12), 5.33 (1H, ddd,  $J = 9.2, 3.9, 0.5$  Hz, H-15), 5.33 (1H, m, H-13), 4.09 (1H, dddd,  $J = 9.6, 8.1, 4.5, 3.3$  Hz, H-3), 3.83 (1H, m, H-7), 3.57 (1H, bs, 3-OH), 2.89 (1H, dq,  $J = 7.4, 7.1$  Hz, H-6), 2.83 (1H, dq,  $J = 8.1, 7.1$  Hz, H-4), 2.70 (3H, s, H-21), 2.64 (1H, m, H-14a), 2.42 (1H, dd,  $J = 14.2, 3.3$  Hz, H-2a), 2.43 (1H, dd,  $J = 14.2, 9.6$  Hz, H-2b), 2.30 (1H, m, H-14b), 2.10 (3H, d,  $J = 1.3$  Hz, H-27), 2.09 (2H, m, H-11), 1.81 (1H, m, H-8), 1.74 (1H, bd,  $J = 5.6$  Hz, 7-OH), 1.53 (1H, m, H-10<sub>β</sub>a), 1.49 (1H, m, H-9<sub>β</sub>), 1.47 (1H, m, H-10<sub>α</sub>a), 1.27 (1H, m, H-10<sub>β</sub>b), 1.24 (1H, m, H-9<sub>α</sub>a), 1.17 (3H, d,  $J = 7.1$  Hz, H-23), 1.14 (1H, m, H-9<sub>α</sub>b), 1.08 (3H, d,  $J = 7.1$  Hz, H-24), 0.97 (3H, d,  $J = 6.9$  Hz, H-25<sub>α</sub>),

0.91 (3H, d,  $J = 6.5$  Hz, H-25<sub>β</sub>), 0.79 (1H, m, H-10<sub>α</sub>b); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ 217.0 (s, C-5), 170.8 (s, C-1), 164.8 (s, C-20), 152.4 (s, C-18), 137.1 (s, C-16), 134.6 (d, C-12), 124.7 (d, C-13), 120.2 (d, C-17), 116.4 (d, C-19), 78.7 (d, C-15), 76.4 (d, C-7), 71.3 (d, C-3), 50.7 (d, C-4), 50.1 (d, C-6), 40.7 (t, C-2), 38.5 (t, C-9<sub>α</sub>), 35.5 (t, C-10<sub>α</sub>), 33.4 (d, C-8), 31.8 (t, C-14), 30.0 (d, C-9<sub>β</sub>), 27.2 (t, C-11), 26.7 (t, C-10<sub>β</sub>), 21.4 (q, C-25<sub>β</sub>), 19.3 (q, C-21), 18.2 (q, C-25<sub>α</sub>), 15.4 (q, C-27), 14.4 (q, C-24), 13.1 (q, C-23); EIMS  $m/z$  505 [M]<sup>+</sup> XXX; HREIMS  $m/z$  505.XXX (calcd. for C<sub>28</sub>H<sub>43</sub>NO<sub>5</sub>S, 505.XXX).

Epothilone I<sub>5</sub> (34): colorless amorphous solid;  $[\alpha]_D^{22}$  -XXX (*c* XXX, MeOH); UV (MeOH)  $\lambda_{\max}$  nm ( $\epsilon$ ) XXX; IR (KBr)  $\nu_{\max}$  XXX cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 6.97 (1H, s, H-19), 6.52 (1H, bs, H-17), 5.32 (1H, dd,  $J = 7.1, 6.2$  Hz, H-15), 5.03 (1H, dd,  $J = 8.4, 5.0$  Hz, H-13), 4.05 (1H, dddd,  $J = 7.5, 7.2, 5.9, 4.6$  Hz, H-3), 3.91 (1H, m, H-7), 3.17 (1H, d,  $J = 5.9$  Hz, 3-OH), 2.94 (1H, dq,  $J = 7.2, 7.1$  Hz, H-4), 2.87 (1H, dq,  $J = 6.5, 6.9$  Hz, H-6), 2.70 (3H, s, H-21), 2.62 (1H, dd,  $J = 14.6, 4.6$  Hz, H-2a), 2.60 (1H, m, H-14a), 2.53 (1H, dd,  $J = 14.6, 7.5$  Hz, H-2b), 2.31 (1H, m, H-14b), 2.10 (3H, d,  $J = 1.1$  Hz, H-27), 2.10 (1H, m, H-11a), 2.02 (1H, m, H-11b), 1.97 (1H, bd,  $J = 5.6$  Hz, 7-OH), 1.84 (1H, m, H-8), 1.66 (3H, s, H-26), 1.55 (1H, m, H-9<sub>β</sub>), 1.49 (1H, m, H-10<sub>β</sub>a), 1.39 (1H, m, H-10<sub>β</sub>b), 1.33 (1H, m, H-10<sub>α</sub>a), 1.31 (1H, m, H-9<sub>α</sub>a), 1.15 (3H, d,  $J = 7.1$  Hz, H-23), 1.12 (1H, m, H-9<sub>α</sub>b), 1.11 (3H, d,  $J = 6.9$  Hz, H-24), 0.97 (3H, d,  $J = 6.9$  Hz, H-25<sub>α</sub>), 0.94 (1H, m, H-10<sub>α</sub>b), 0.93 (3H, d,  $J = 6.6$  Hz, H-25<sub>β</sub>); EIMS  $m/z$  519 [M]<sup>+</sup> XXX; HREIMS  $m/z$  519.XXX (calcd. for C<sub>29</sub>H<sub>45</sub>NO<sub>5</sub>S, 519.XXX).

Epothilone I<sub>6</sub> (35): colorless amorphous solid;  $[\alpha]_D^{22}$  -XXX (*c* XXX, MeOH); UV (MeOH)  $\lambda_{\max}$  nm ( $\epsilon$ ) XXX; IR (KBr)  $\nu_{\max}$  XXX cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 6.97 (1H,

s, H-19), 6.52 (1H, bs, H-17), 5.24 (1H, dd,  $J = 6.9$ , 6.9 Hz, H-15), 5.02 (1H, dd,  $J = 8.8$ , 5.2 Hz, H-13), 4.22 (1H, tdd,  $J = 6.1$ , 5.6, 4.8 Hz, H-3), 3.76 (1H, ddd,  $J = 6.1$ , 5.7, 5.6 Hz, H-7), 3.13 (1H, d,  $J = 5.6$  Hz, 3-OH), 3.05 (1H, dq,  $J = 4.8$ , 7.0 Hz, H-4), 2.79 (1H, dq,  $J = 5.6$ , 6.9 Hz, H-6), 2.70 (3H, s, H-21), 2.62 (1H, m, H-14a), 2.57 (2H, d,  $J = 6.1$  Hz, H-2a), 2.30 (1H, m, H-14b), 2.08 (3H, d,  $J = 1.0$  Hz, H-27), 2.02 (2H, m, H-11), 1.73 (1H, d,  $J = 6.1$  Hz, 7-OH), 1.69 (1H, m, H-8), 1.66 (3H, s, H-26), **XXX (H-9 $_{\alpha}$ , H-9 $_{\beta}$ , H-10 $_{\alpha}$ , H-10 $_{\beta}$ )**, 1.21 (3H, d,  $J = 7.0$  Hz, H-22), 1.16 (3H, d,  $J = 6.9$  Hz, H-24), 0.94 (3H, d,  $J = 6.9$  Hz, H-25 $_{\alpha}$ ), 0.91 (3H, d,  $J = 6.4$  Hz, H-25 $_{\beta}$ ); **EIMS  $m/z$  519 [M] $^{+}$  XXX; HREIMS  $m/z$  519.XXX (calcd. for C<sub>29</sub>H<sub>45</sub>NO<sub>5</sub>S, 519.XXX).**

**Epothilone K (36):** colorless amorphous solid;  $[\alpha]^{22}_D -7$  (*c* 0.08, MeOH); UV (MeOH)  $\lambda_{\max}$  nm ( $\epsilon$ ) 212 (16700), 248 (12500); IR (KBr)  $\nu_{\max}$  3431, 2963, 2927, 2856, 1731, 1712, 1262, 1093, 1021, 802 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  6.95 (1H, s, H-19), 6.51 (1H, bs, H-17), 5.49 (3H, m, H-15, H-13, and H-12), 4.04 (1H, dddd,  $J = 7.9$ , 7.6, 6.9, 3.3 Hz, H-3), 3.36 (1H, dq,  $J = 6.9$ , 6.8 Hz, H-6), 2.83 (1H, d,  $J = 7.6$  Hz, 3-OH), 2.75 (1H, ddd,  $J = 16.1$ , 6.6, 3.4 Hz, H-14a), 2.74 (1H, dd,  $J = 15.3$ , 3.3 Hz, H-2a), 2.71 (3H, s, H-21), 2.58 (2H, m, H-14b and H-8), 2.50 (1H, dd,  $J = 15.3$ , 7.9 Hz, H-2b), 2.29 (1H, m, H-11a), 2.10 (1H, m, H-11b), 2.09 (3H, d,  $J = 0.7$  Hz, H-27), 1.78 (1H, m, H-9a), 1.65 (1H, m, H-10a), 1.48 (1H, m, H-10b), 1.18 (1H, m, H-9b), 1.15 (3H, d,  $J = 6.8$  Hz, H-22), 1.03 (3H, d,  $J = 6.5$  Hz, H-25); **EIMS  $m/z$  405 [M] $^{+}$  (38), 317 (12), 260 (9), 232 (10), 204 (14), 190 (16), 168 (100), 164 (30), 151 (28); HREIMS  $m/z$  405.XXX (calcd. for C<sub>26</sub>H<sub>39</sub>NO<sub>5</sub>S, 405.XXX).**

**(37):** colorless amorphous solid;  $[\alpha]^{22}_D -27.5$  (*c* 0.4, MeOH); UV (MeOH)  $\lambda_{\max}$  nm ( $\epsilon$ )

211 (16100), 247 (12100); IR (KBr)  $\nu_{\max}$  3431, 2967, 2929, 2875, 1704, 1462, 1381, 1010  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  6.94 (1H, s, H-19), 6.55 (1H, bs, H-17), 5.56 (1H, dtt,  $J = 10.8$ , 7.3, 1.4 Hz, H-12), 5.39 (1H, dtt,  $J = 10.8$ , 7.3, 1.4 Hz, H-13), 4.17 (1H, t,  $J = 6.6$  Hz, H-15), 3.50 (1H, ddd,  $J = 8.7$ , 2.6, 2.6 Hz, H-7), 3.10 (1H, d,  $J = 2.6$ , 7-OH), 2.90 (1H, dq,  $J = 2.6$ , 7.2 Hz, H-6), 2.77 (1H, sep,  $J = 6.9$  Hz, H-4), 2.70 (3H, s, H-21), 2.40 (2H, m, H-14), 2.07 (2H, m, H-11), 2.04 (3H, d,  $J = 1.1$  Hz, H-27), 1.78 (1H, bs, 15-OH), 1.74 (1H, m, H-9a), 1.50 (1H, m, H-8), 1.46 (1H, m, H-10a), 1.27 (1H, m, H-10b), 1.11 (1H, m, H-9b), 1.094 (3H, d,  $J = 6.9$  Hz, H-23), 1.089 (3H, d,  $J = 6.9$  Hz, H-22), 1.08 (3H, d,  $J = 7.2$  Hz, H-24), 0.82 (3H, d,  $J = 6.7$  Hz, H-25);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  220.5 (s, C-5), 164.6 (s, C-20), 152.9 (s, C-18), 141.5 (s, C-16), 133.4 (d, C-12), 125.0 (d, C-13), 119.2 (d, C-17), 115.6 (d, C-19), 77.2 (d, C-15), 74.9 (d, C-7), 44.9 (d, C-6), 40.0 (d, C-4), 35.5 (d, C-8), 33.5 (t, C-14), 32.3 (t, C-9), 27.9 (t, C-11), 26.9 (t, C-10), 19.2 (q, C-21), 18.6 (q, C-23), 18.1 (q, C-22), 15.6 (q, C-25), 14.4 (q, C-27), 9.3 (q, C-24); EIMS  $m/z$  407  $[\text{M}]^+$  (0.1), 204 (0.8), 168 (100), 140 (3.4); HREIMS  $m/z$  407.XXX (calcd. for  $\text{C}_{23}\text{H}_{37}\text{NO}_3\text{S}$ , 407.XXX).

(38): colorless amorphous solid;  $[\alpha]_{\text{D}}^{22} +25.0$  (c 0.5, MeOH); UV (MeOH)  $\lambda_{\max}$  nm ( $\epsilon$ ) 212 (17700), 247 (13400); IR (KBr)  $\nu_{\max}$  3427, 2971, 2933, 2878, 2858, 1709, 1457, 1377, 1186, 1023  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  6.95 (1H, s, H-19), 6.55 (1H, bs, H-17), 5.52 (1H, dtt,  $J = 10.9$ , 7.2, 1.4 Hz, H-12), 5.39 (1H, dtt,  $J = 10.9$ , 7.1, 1.2 Hz, H-13), 4.18 (1H, ddt,  $J = 3.4$ , 0.4, 6.7 Hz, H-15), 2.71 (3H, s, H-21), 2.51 (1H, bq,  $J = 6.8$  Hz, H-8), 2.48 (1H, dq,  $J = 17.7$ , 7.4 Hz, H-6a), 2.41 (1H, dq,  $J = 17.7$ , 7.2 Hz, H-6b), 2.39 (2H, ddd,  $J = 7.1$ , 6.7, 1.4 Hz, H-14), 2.06 (2H, ddt, 7.2, 1.2, 7.0 Hz, H-11), 2.05 (3H, d,  $J = 1.4$  Hz, H-27), 1.81 (1H, d,  $J = 3.4$  Hz,

15-OH), 1.66 (1H, m, H-9a), 1.32 (1H, m, H-9b), 1.31 (2H, m, H-10), 1.06 (3H, d,  $J = 6.9$  Hz, H-25), 1.04 (3H, dd,  $J = 7.4, 7.2$  Hz, H-24);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  215.3 (s, C-7), 164.6 (s, C-20), 152.9 (s, C-18), 141.5 (s, C-16), 132.7 (d, C-12), 125.3 (d, C-13), 119.2 (d, C-17), 115.6 (d, C-19), 77.2 (d, C-15), 46.0 (d, C-8), 34.3 (t, C-14), 33.5 (t, C-6), 32.7 (t, C-9), 27.5 (t, C-11), 27.3 (t, C-10), 19.2 (q, C-21), 16.5 (q, C-25), 14.4 (q, C-27), 7.8 (q, C-24); EIMS  $m/z$  335  $[\text{M}]^+$  (2), 317 (4), 170 (27), 169 (67), 168 (100), 140 (20); HREIMS  $m/z$  335.1912 (calcd. for  $\text{C}_{19}\text{H}_{29}\text{NO}_2\text{S}$ , 335.1919).

(39): colorless amorphous solid;  $[\alpha]_D^{22} +26.4$  ( $c$  0.27, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) 203 (19100), 244 (12500); IR (KBr)  $\nu_{\text{max}}$  3430, 2970, 2934, 2877, 1710, 1458, 1377, 1184  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  6.94 (1H, s, H-19), 6.55 (1H, bs, H-17), 5.17 (1H, t,  $J = 7.3$  Hz, H-13), 4.13 (1H, m, H-15), 2.70 (3H, s, H-21), 2.51 (1H, bq,  $J = 6.8$  Hz, H-8), 2.47 (1H, dq,  $J = 17.7, 7.2$  Hz, H-6a), 2.41 (1H, dq,  $J = 17.7, 7.2$  Hz, H-6b), 2.33 (2H, bdd,  $J = 7.3, 6.8$  Hz, H-14), 2.05 (3H, d,  $J = 1.2$  Hz, H-27), 2.03 (2H, m, H-11), 1.71 (1H, d,  $J = 3.2$  Hz, 15-OH), 1.69 (3H, d,  $J = 1.3$  Hz, H-26), 1.62 (1H, m, H-9a), 1.32 (3H, m, H-10 and H-9b), 1.06 (3H, d,  $J = 6.9$  Hz, H-25), 1.03 (3H, t,  $J = 7.2$  Hz, H-24); EIMS  $m/z$  349  $[\text{M}]^+$  (0.7), 331 (1.7), 168 (100), 140 (5.1); HREIMS  $m/z$  349.XXX (calcd. for  $\text{C}_{20}\text{H}_{31}\text{NO}_2\text{S}$ , 349.XXX).

Tab 1. Aktivität von Epothilonen und Verbindungen (1) bis (39) gegen Maus-Fibroblasten (L929, IC50 /ng/ml/)

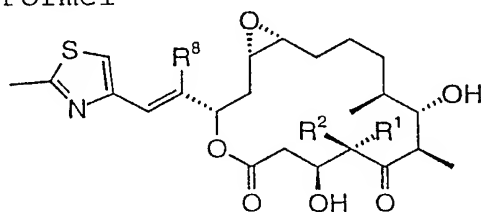
Struktur- typ	Epothilone				
	A <sub>Y</sub>	B <sub>Y</sub>	C <sub>Y</sub>	D <sub>Y</sub>	trans C <sub>Y</sub>
Ausgangs- epothilon	(1) 4	(2) 1-2	(14) 50-100	(15) 20	-
21-Hydroxy (E&F)	(3) 10	(4) 1.5	-	-	-
Oxazoles (G&H)	(10) 6	(11) 1	(12) 120	(13) 11	-
(R)-4-Desmethyl (X <sub>1</sub> )	(5) 20	-	(16) 200	(17) 20	(28) 400
(S)-4-Desmethyl (X <sub>2</sub> )	(6) 7	-	(18) 25-30	(19) 12	(29) 80
6-Desmethyl (X <sub>3</sub> )	-	-	(20) 1500	-	-
8-Desmethyl (X <sub>4</sub> )	-	-	(21) 800	-	-
8,9-Dehydro (X <sub>5</sub> )	-	-	(22) 1500	(23) 200	-
10,11-Dehydro (X <sub>6</sub> )	-	-	(24) 120	-	-
14-Hydroxy (X <sub>7</sub> )	-	-	(25)	-	-
16-Desmethyl (X <sub>8</sub> )	(7) 20	-	(26) 250	-	-
27-Hydroxy (X <sub>9</sub> )	(8) 100	-	(27) 200	-	-
21-Methyl (X <sub>10</sub> )	-	(9) 1.5	-	-	-
Verbindung	-	-	(36) 180		
Verbindung	-	-	(37) 50	-	-
Verbindung	-	-	(38) 2000	(39) 500	-

# Epothilon-Nebenkomponenten

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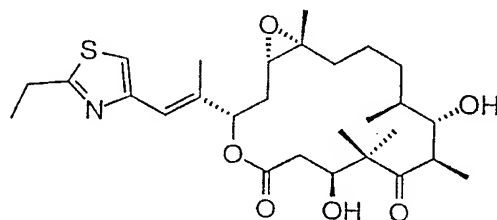
## Patentansprüche

### 1. Epothilon der Formel



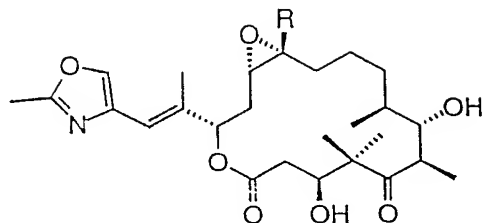
- Epothilone A<sub>1</sub> (5) R<sup>1</sup> = H; R<sup>2</sup>, R<sup>8</sup> = Me  
 Epothilone A<sub>2</sub> (6) R<sup>2</sup> = H; R<sup>1</sup>, R<sup>8</sup> = Me  
 Epothilone A<sub>8</sub> (7) R<sup>8</sup> = H; R<sup>1</sup>, R<sup>2</sup> = Me      oder  
 Epothilone A<sub>9</sub> (8) R<sup>1</sup> = CH<sub>2</sub>OH; R<sup>2</sup>, R<sup>8</sup> = Me

### 2. Epothilon der Formel



Epothilone B<sub>10</sub> (9)

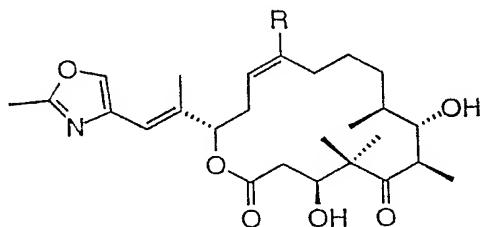
## 3. Epothilon der Formel



- ✓ Epothilone G<sub>1</sub> (10) R = H  
 ✓ Epothilone G<sub>2</sub> (11) R = Me

oder

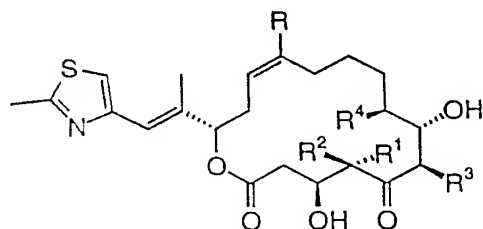
## 4. Epothilon der Formel



- ✓ Epothilone H<sub>1</sub> (12) R = H  
 ✓ Epothilone H<sub>2</sub> (13) R = Me

oder

## 5. Epothilon der Formel

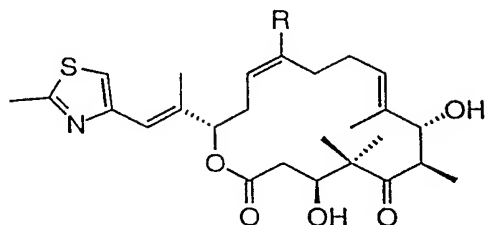


- ✓ Epothilone C<sub>1</sub> (16) R<sup>1</sup> = H; R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup> = Me; R = H  
 ✓ Epothilone D<sub>1</sub> (17) R<sup>1</sup> = H; R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup> = Me; R = Me  
 ✓ Epothilone C<sub>2</sub> (18) R<sup>2</sup> = H; R<sup>1</sup>, R<sup>3</sup>, R<sup>4</sup> = Me; R = H  
 ✓ Epothilone D<sub>2</sub> (19) R<sup>2</sup> = H; R<sup>1</sup>, R<sup>3</sup>, R<sup>4</sup> = Me; R = Me  
 ✓ Epothilone C<sub>3</sub> (20) R<sup>3</sup> = H; R<sup>1</sup>, R<sup>2</sup>, R<sup>4</sup> = Me; R = H  
 ✓ Epothilone C<sub>4</sub> (21) R<sup>4</sup> = H; R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup> = Me; R = H

oder

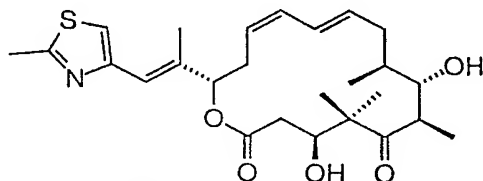


## 6. Epothilon der Formel

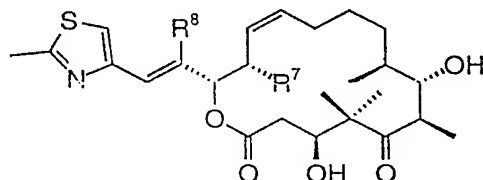
Epothilone C<sub>5</sub> (22) R = HEpothilone D<sub>5</sub> (23) R = Me

oder

## 7. Epothilon der Formel

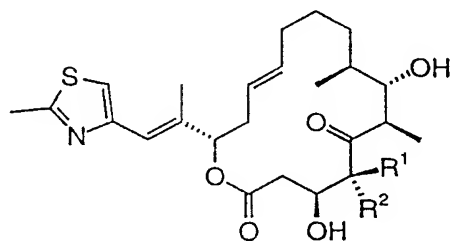
✓ Epothilone C<sub>6</sub> (24)

## 8. Epothilin der Formel

✓ Epothilone C<sub>7</sub> (25) R<sup>7</sup> = OH; R<sup>8</sup> = Me✓ Epothilone C<sub>8</sub> (26) R<sup>8</sup>, R<sup>7</sup> = H✓ Epothilone C<sub>9</sub> (27) R<sup>8</sup> = CH<sub>2</sub>OH; R<sup>7</sup> = H

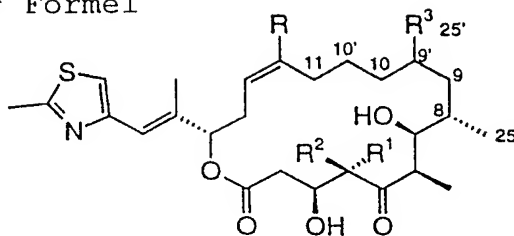
oder

## 9. Epothilon der Formel

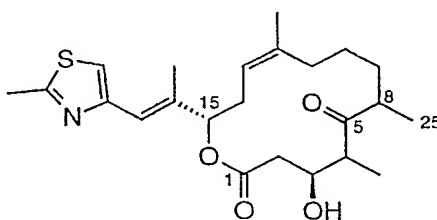
✓ trans-Epothilone C<sub>1</sub> (28) R<sup>1</sup> = H; R<sup>2</sup> = Me✓ trans-Epothilone C<sub>2</sub> (29) R<sup>2</sup> = H; R<sup>1</sup> = Me

oder

## 10. Epothilon der Formel

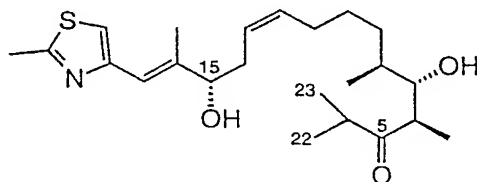
Epothilone I<sub>1</sub> (30) R, R<sup>3</sup> = H; R<sup>1</sup>, R<sup>2</sup> = MeEpothilone I<sub>2</sub> (31) R = H; R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup> = MeEpothilone I<sub>3</sub> (32) R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R = MeEpothilone I<sub>4</sub> (33) R<sup>2</sup>, R = H; R<sup>1</sup>, R<sup>3</sup> = MeEpothilone I<sub>5</sub> (34) R<sup>2</sup> = H; R<sup>1</sup>, R<sup>3</sup>, R = Me oderEpothilone I<sub>6</sub> (35) R<sup>1</sup> = H; R<sup>2</sup>, R<sup>3</sup>, R = Me

## 11. Epothilon der Formel



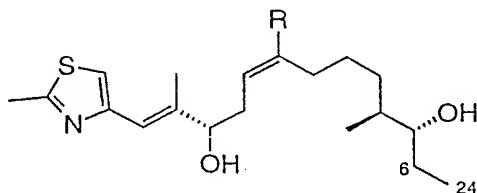
✓ Epothilone K (36)

## 12. Verbindung der Formel



(37)

## 13. Verbindung der Formel



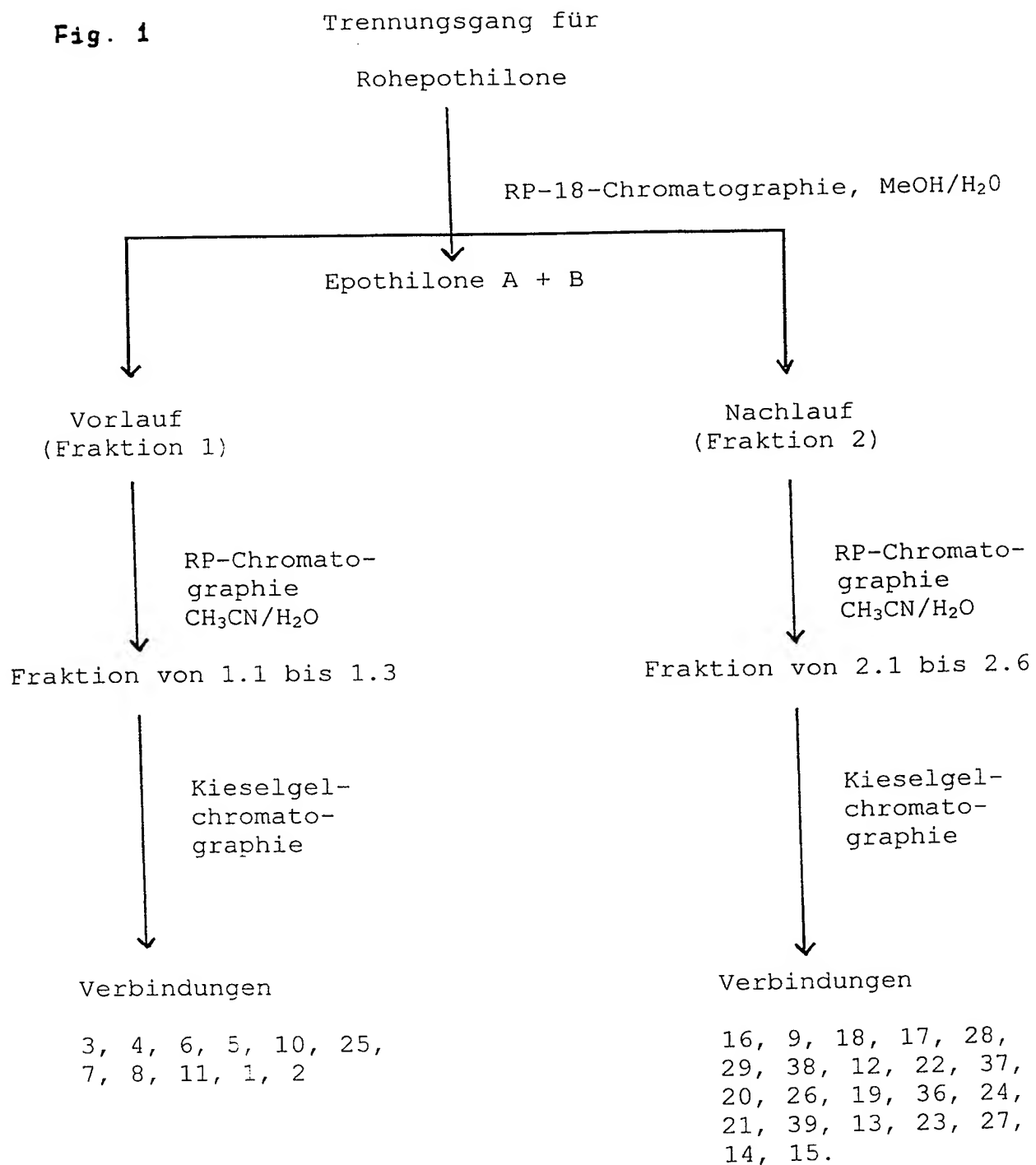
(38) R = H

(39) R = Me

oder

1/2

Fig. 1



2/2

Fig. 2

		Epothilone E (3)	variable <sup>a</sup>
		Epothilone F (4)	variable <sup>a</sup>
fraction 1	1.1	Epothilone A <sub>2</sub> (6)	14.5 mg
		Epothilone A <sub>1</sub> (5)	3.1 mg
		Epothilone G <sub>1</sub> (10)	52.3 mg
		Epothilone C <sub>7</sub> (25)	0.9 mg
		Epothilone A <sub>8</sub> (7)	38.7 mg
	1.2	Epothilone A <sub>9</sub> (8)	4.4 mg
		Epothilone G <sub>2</sub> (11)	9.4 mg
	1.3	Epothilone A (1)	29800.0 mg
		Epothilone B (2)	10300.0 mg
fraction 2	2.1	Epothilone C <sub>1</sub> (16)	32.4 mg
		Epothilone B <sub>10</sub> (9)	1.1 mg
	2.2	Epothilone C <sub>2</sub> (18)	58.4 mg
		Epothilone D <sub>1</sub> (17)	5.3 mg
	2.3	trans-Epothilone C <sub>1</sub> (28)	1.4 mg
		trans-Epothilone C <sub>2</sub> (29)	4.5 mg
		38	6.5 mg
		Epothilone H <sub>1</sub> (12)	3.0 mg
		Epothilone C <sub>5</sub> (22)	7.3 mg
	2.4	37	2.9 mg
		Epothilone C <sub>3</sub> (20)	32.5 mg
		Epothilone C <sub>8</sub> (26)	26.3 mg
		Epothilone D <sub>2</sub> (19)	13.1 mg
		Epothilone K (36)	0.4 mg
	2.5	Epothilone C <sub>6</sub> (24)	2.9 mg
		Epothilone C <sub>4</sub> (21)	6.5 mg
		39	0.8 mg
	2.6	Epothilone H <sub>2</sub> (13)	1.5 mg
		Epothilone D <sub>5</sub> (23)	0.9 mg
		Epothilone C <sub>9</sub> (27)	3.0 mg
		Epothilone C (14)	4600.0 mg
		Epothilone D (15)	2700.0 mg